with Thiophosgene - Conversion to Isothiocyanate Groups
An aqueous solution of the product prepared in Example 2 is added to an equal volume. . .

The procedure is repeated, substituting the product of Example 3 for the product of Example 2,
EXAMPLE 5
Activation of Amino Group of DOTA-N(2-Aminoethyl)Amide with Bromoacetyl Chloride - Conversion to Bromoacetamide Grou'ps
An aqueous solution of the product prepared in Example 2 (20mg/ml) which also contains triethylamine (20mg/ml) is. . .

EXAMPLE 13
Preparation of - PAMAM - Poly DOTA
The G2.0 PAMAM dendrimer prepared in Example 10 (log, 0.01 mol) is combined with 12 equivalents of DOTA carboxycarbonic anhydride (0,13 mol) prepared as in Example 1, by slowly mixing a precooled (00 C) acetonitrile solution (20 ml) of dendrimer to the DOTA mixed anhydride slurry over 10 minutes and gradually allowing the reaction mixture to warm to ambient temperature. The reaction mixture is worked up. . .

EXAMPLE 17
Preparation of DOTA-G3 Dendrimer magnifier
An acetonitrile solution of tris-t-butyl-DO3A and ClCH2CONHCH2(C6H4)pNO2 (Example 16) are heated at 65DC for 24 hours, The chelant-linker product is isolated. . .

CLMEN. . . compound according to any one of claims 1 to 13 wherein said macrocyclic chelants are selected from the residues of 1,4,7,10- tetraazacyclododecanetetraacetic acid (DOTA),
1 7,10-tetraazacyclododecane 4 triacetic acid (DO3A), I-oxa 7,10-triazacyclododecane-triacetic acid (DOXA), 1 7-triazacyclononanetriacetic acid (NOTA), 11408fll-tetraazacyclotetradecanetetraacetic acid (TETA), DOTA-N(2-aminoethyl)amide and DOTA-N(4-aminophenethyl)amide.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	74.85	210.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-3.00

STN INTERNATIONAL LOGOFF AT 14:05:21 ON 07 DEC 2006

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LOGINID:SSSPTA1642BJF

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	AUG 09	INSPEC enhanced with 1898-1968 archive
NEWS 4	AUG 28	ADISCTI Reloaded and Enhanced
NEWS 5	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 6	SEP 11	CA/CAplus enhanced with more pre-1907 records
NEWS 7	SEP 21	CA/CAplus fields enhanced with simultaneous left and right truncation
NEWS 8	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 9	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 10	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 11	SEP 28	CEABA-VTB classification code fields reloaded with new classification scheme
NEWS 12	OCT 19	LOGOFF HOLD duration extended to 120 minutes
NEWS 13	OCT 19	E-mail format enhanced
NEWS 14	OCT 23	Option to turn off MARPAT highlighting enhancements available
NEWS 15	OCT 23	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 16	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 17	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 18	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 19	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 20	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 21	NOV 13	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 22	NOV 20	CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS 23	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 24	NOV 20	CA/CAplus patent kind codes will be updated
NEWS 25	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 26	DEC 11	CAS REGISTRY chemical nomenclature enhanced

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

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     as well as in synaptic membranes.
IT   6667-50-1   17650-98-5   20988-63-0 25126-32-3
     25679-24-7   35144-91-3   78137-39-0   78151-11-8
     RL: PRP (Properties)
        (degradation of, by brain synaptosomes)


=> d his

     (FILE 'HOME' ENTERED AT 13:35:48 ON 07 DEC 2006)

     FILE 'REGISTRY' ENTERED AT 13:36:14 ON 07 DEC 2006
L1           136 S DY'NLE'GW'NLE'DF/SQSP
L2           424 S DYMGWMDF/SQSP

     FILE 'CAPLUS' ENTERED AT 13:39:00 ON 07 DEC 2006
L3            84 S L1
L4             0 S DPTA AND L3
L5             5 S DOTA AND L3
L6        134722 S CHELAT?
L7            12 S L6 AND L3
L8             0 S L7 NOT PY>1997
L9             1 S L7 NOT PY>1998
L10         4485 S L2
L11           49 S L10 AND L6
L12           20 S L11 NOT PY>1997
L13           20 S L11 NOT PY>1996
L14        14458 S METAL CHELAT?
L15            3 S L14 AND L10

=> s l10 and (DPTA or DOTA)
            347 DPTA
              1 DPTAS
            347 DPTA
                  (DPTA OR DPTAS)
           1203 DOTA
L16            4 L10 AND (DPTA OR DOTA)

=> d ibib 1-4

L16  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2004:702005  CAPLUS
DOCUMENT NUMBER:          141:230668
TITLE:                    Contrast enhanced x-ray phase imaging
INVENTOR(S):              Mattiuzzi, Marco; Arfelli, Fulvia; Menk, Ralf-Hendrik;
                          Rigon, Luigi; Besch, Hans-Juergen
PATENT ASSIGNEE(S):       Bracco Imaging S.P.A., Italy
SOURCE:                   PCT Int. Appl., 38 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    -------------------      --------
     WO 2004071535         A1    20040826    WO 2004-EP1213           20040210
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
             BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
             MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG
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EP 1592456	A1	20051109	EP 2004-709594	20040210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006517558	T2	20060727	JP 2006-501789	20040210
PRIORITY APPLN. INFO.:			US 2003-446986P	P 20030213
			WO 2004-EP1213	W 20040210

L16 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:43075 CAPLUS
DOCUMENT NUMBER: 135:118839
TITLE: Use of the rat pancreatic CA20948 cell line for the comparison of radiolabelled peptides for receptor-targeted scintigraphy and radionuclide therapy
AUTHOR(S): Bernard, B. F.; Krenning, E.; Breeman, W. A. P.; Visser, T. J.; Bakker, W. H.; Srinivasan, A.; De Jong, M.
CORPORATE SOURCE: Departments of Nuclear Medicine, University Hospital Dijkzigt, Rotterdam, 3015 GD, Neth.
SOURCE: Nuclear Medicine Communications (2000), 21(11), 1079-1085
CODEN: NMCODC; ISSN: 0143-3636
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:271563 CAPLUS
DOCUMENT NUMBER: 129:119669
TITLE: Unsulfated DTPA- and DOTA-CCK analogs as specific high-affinity ligands for CCK-B receptor-expressing human and rat tissues in vitro and in vivo
AUTHOR(S): Reubi, J. C.; Waser, B.; Schaer, J. C.; Laederach, U.; Erion, J.; Srinivasan, A.; Schmidt, M. A.; Bugaj, J. E.
CORPORATE SOURCE: Institute of Pathology, Division of Cell Biology and Experimental Cancer Research, University of Berne, Switz.
SOURCE: European Journal of Nuclear Medicine (1998), 25(5), 481-490
CODEN: EJNMD9; ISSN: 0340-6997
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:594650 CAPLUS
DOCUMENT NUMBER: 127:259530
TITLE: Use of labeled CCK-B receptor ligands for the detection, localization, and treatment of malignant human tumors
INVENTOR(S): Reubi, Jean-Claude
PATENT ASSIGNEE(S): Mallinckrodt Medical, Inc., USA; Reubi, Jean-Claude
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9731657	A2	19970904	WO 1997-US3056		19970225
WO 9731657	A3	19971023			
W: CA, JP, US					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
CA 2247430	AA	19970904	CA 1997-2247430		19970225
EP 885017	A2	19981223	EP 1997-908751		19970225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2000506141	T2	20000523	JP 1997-531108		19970225
US 2004185510	A1	20040923	US 2003-626229		20030724
PRIORITY APPLN. INFO.:			EP 1996-200498	A	19960227
			WO 1997-US3056	W	19970225
			US 1999-125823	B1	19990119
OTHER SOURCE(S):	MARPAT 127:259530				

```
=> s l10 and DTPA
          9401 DTPA
             6 DTPAS
          9401 DTPA
                 (DTPA OR DTPAS)
L17          9 L10 AND DTPA

=> d ibib 1-9
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L17 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2004:424231 CAPLUS
DOCUMENT NUMBER:	141:271813
TITLE:	Synthesis and characterization of a sulfated and a non-sulfated cyclic CCK8 analogue functionalized with a chelating group for metal labelling
AUTHOR(S):	De Luca, Stefania; Morelli, Giancarlo
CORPORATE SOURCE:	Centro Interuniversitario per la Ricerca sui Peptidi Bioattivi (CIRPeB) and Dipartimento di Chimica Biologica, Universita di Napoli "Federico II", Naples, 80134, Italy
SOURCE:	Journal of Peptide Science (2004), 10(5), 265-273 CODEN: JPSIEI; ISSN: 1075-2617
PUBLISHER:	John Wiley & Sons Ltd.
DOCUMENT TYPE:	Journal
LANGUAGE:	English
REFERENCE COUNT:	13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2004:254192 CAPLUS
DOCUMENT NUMBER:	142:62411
TITLE:	In Vitro and In Vivo Characterization of Indium-111 and Technetium-99m Labeled CCK-8 Derivatives for CCK-B Receptor Imaging
AUTHOR(S):	Aloj, L.; Panico, M.; Caraco, C.; Del Vecchio, S.; Arra, C.; Affuso, A.; Accardo, A.; Mansi, R.; Tesauro, D.; De Luca, S.; Pedone, C.; Visentin, R.; Mazzi, U.; Morelli, G.; Salvatore, M.
CORPORATE SOURCE:	Istituto di Biostrutture e Bioimmagini, CNR, Naples, Italy
SOURCE:	Cancer Biotherapy & Radiopharmaceuticals (2004), 19(1), 93-98 CODEN: CBRAFJ; ISSN: 1084-9785
PUBLISHER:	Mary Ann Liebert, Inc.
DOCUMENT TYPE:	Journal
LANGUAGE:	English
REFERENCE COUNT:	16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:133309 CAPLUS
DOCUMENT NUMBER: 138:197782
TITLE: Peptides conjugates, their derivatives with metal complexes and use thereof for magnetic resonance imaging (MRI)
INVENTOR(S): Aime, Silvio; Gianolio, Eliana; Morelli, Giancarlo; Pedone, Carlo; Tesauro, Diego; Lattuada, Luciano; Visigalli, Massimo; Anelli, Pier Lucio
PATENT ASSIGNEE(S): Bracco Imaging S.P.A., Italy
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014157	A2	20030220	WO 2002-EP8382	20020726
WO 2003014157	A3	20031113		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002328981	A1	20030224	AU 2002-328981	20020726
EP 1412383	A2	20040428	EP 2002-764797	20020726
EP 1412383	B1	20061115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005510461	T2	20050421	JP 2003-519106	20020726
US 2005008573	A1	20050113	US 2004-485847	20040902
PRIORITY APPLN. INFO.:			IT 2001-MI1708 A	20010803
			WO 2002-EP8382 W	20020726

OTHER SOURCE(S): MARPAT 138:197782

L17 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:609701 CAPLUS
DOCUMENT NUMBER: 136:321340
TITLE: New radiolabeled CCK-8 analogues [Tc-99m-GH-CCK-8 and Tc-99m-DTPA-CCK-8]: preparation and biodistribution studies in rats and rabbits
AUTHOR(S): Ertay, T.; Unak, P.; Bekis, R.; Yurt, F.; Biber, F. Z.; Durak, H.
CORPORATE SOURCE: Dept. of Nuclear Medicine, Dokuz Eylul University, Medical School, Inciralti, Izmir, Turk.
SOURCE: Nuclear Medicine and Biology (2001), 28(6), 667-678
CODEN: NMBIEO; ISSN: 0969-8051
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:402924 CAPLUS
DOCUMENT NUMBER: 131:225550

TITLE: Radiolabeled peptides for targeting cholecystokinin-B/gastrin receptor-expressing tumors
AUTHOR(S): Behr, Thomas M.; Jenner, Niels; Behe, Martin; Angerstein, Christa; Gratz, Stefan; Raue, Friedhelm; Becker, Wolfgang
CORPORATE SOURCE: Department of Nuclear Medicine, Georg-August-University, Gottingen, D-37075, Germany
SOURCE: Journal of Nuclear Medicine (1999), 40(6), 1029-1044
CODEN: JNMEAQ; ISSN: 0161-5505
PUBLISHER: Society of Nuclear Medicine, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:396519 CAPLUS
DOCUMENT NUMBER: 131:200015
TITLE: Tri-t-butyl-DTPA: a versatile synthon for the preparation of DTPA-containing peptides by solid phase
AUTHOR(S): Srinivasan, Ananth; Schmidt, Michelle A.
CORPORATE SOURCE: Mallinckrodt Inc., Hazelwood, MO, 63042, USA
SOURCE: Peptides: Frontiers of Peptide Science, Proceedings of the American Peptide Symposium, 15th, Nashville, June 14-19, 1997 (1999), Meeting Date 1997, 267-268.
Editor(s): Tam, James P.; Kaumaya, Pravin T. P.
Kluwer: Dordrecht, Neth.
CODEN: 67UCAR
DOCUMENT TYPE: Conference
LANGUAGE: English
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:271563 CAPLUS
DOCUMENT NUMBER: 129:119669
TITLE: Unsulfated DTPA- and DOTA-CCK analogs as specific high-affinity ligands for CCK-B receptor-expressing human and rat tissues in vitro and in vivo
AUTHOR(S): Reubi, J. C.; Waser, B.; Schaer, J. C.; Laederach, U.; Erion, J.; Srinivasan, A.; Schmidt, M. A.; Bugaj, J. E.
CORPORATE SOURCE: Institute of Pathology, Division of Cell Biology and Experimental Cancer Research, University of Berne, Switz.
SOURCE: European Journal of Nuclear Medicine (1998), 25(5), 481-490
CODEN: EJNMD9; ISSN: 0340-6997
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:594650 CAPLUS
DOCUMENT NUMBER: 127:259530
TITLE: Use of labeled CCK-B receptor ligands for the detection, localization, and treatment of malignant human tumors
INVENTOR(S): Reubi, Jean-Claude
PATENT ASSIGNEE(S): Mallinckrodt Medical, Inc., USA; Reubi, Jean-Claude
SOURCE: PCT Int. Appl., 61 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9731657	A2	19970904	WO 1997-US3056		19970225
WO 9731657	A3	19971023			
W: CA, JP, US					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
CA 2247430	AA	19970904	CA 1997-2247430		19970225
EP 885017	A2	19981223	EP 1997-908751		19970225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2000506141	T2	20000523	JP 1997-531108		19970225
US 2004185510	A1	20040923	US 2003-626229		20030724
PRIORITY APPLN. INFO.:			EP 1996-200498	A	19960227
			WO 1997-US3056	W	19970225
			US 1999-125823	B1	19990119

OTHER SOURCE(S): MARPAT 127:259530

L17 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:69756 CAPLUS
DOCUMENT NUMBER: 110:69756
TITLE: Effects of cholecystokinin-octapeptide (CCK-8) on food intake and gastric emptying in man
AUTHOR(S): Muurahainen, Norma; Kissileff, Harry R.; Derogatis, Andrew J.; Xavier Pi Sunyer, F.
CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, 10025, USA
SOURCE: Physiology & Behavior (1988), 44(4-5), 645-9
CODEN: PHBHA4; ISSN: 0031-9384
DOCUMENT TYPE: Journal
LANGUAGE: English

=> d kwic 9

L17 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
AB . . . infusions of CCK-8 and saline on sep. nonconsecutive days after they had consumed 500 g of tomato soup tagged with technetium-99-DTPA. Intake of a test meal was measured 20 min after consumption of the soup whereas gastric emptying was simultaneously monitored. . .
IT 25126-32-3
RL: BIOL (Biological study)
(appetite and stomach emptying response to, in man)

=> file dissab

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	69.02	128.33
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.00	-3.00

FILE 'DISSABS' ENTERED AT 13:46:43 ON 07 DEC 2006

FILE COVERS 1861 TO 27 NOV 2006 (20061127/ED)

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```
=> s cholecystokinin or (CCK-8 or CCK8 or CCK () 8))
UNMATCHED RIGHT PARENTHESIS '8))'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s cholecystokinin or (CCK-8 or CCK8 or (CCK () 8))
           307 CHOLECYSTOKININ
           299 CCK
             1 CCKS
           299 CCK
                 (CCK OR CCKS)
         85654 8
            65 CCK-8
                 (CCK(W)8)
            13 CCK8
           299 CCK
             1 CCKS
           299 CCK
                 (CCK OR CCKS)
         85654 8
            65 CCK (W) 8
L18        323 CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK (W) 8))

=> s DTPA or DOTA
           330 DTPA
            38 DOTA
L19        360 DTPA OR DOTA

=> s l19 and l18
L20          2 L19 AND L18

=> d ibib 1-2

L20  ANSWER 1 OF 2  DISSABS COPYRIGHT (C) 2006 ProQuest Information and
     Learning Company; All Rights Reserved on STN
ACCESSION NUMBER:   96:28812  DISSABS   Order Number: AAIMM03308
TITLE:              POLYAMINOPOLYCARBOXYLIC ACIDS FOR RADIOLABELLING SMALL
                    DRUGS
AUTHOR:             BARLOW, STEPHEN ROBERT [M.SC.]; HUNTER, DUNCAN H. [advisor]
CORPORATE SOURCE:   THE UNIVERSITY OF WESTERN ONTARIO (CANADA) (0784)
SOURCE:             Masters Abstracts International, (1995) Vol. 34, No. 3, p.
                    1181. Order No.: AAIMM03308. 137 pages.
                    ISBN: 0-612-03308-2.
DOCUMENT TYPE:      Dissertation
FILE SEGMENT:       MAI
LANGUAGE:           English
ENTRY DATE:         Entered STN: 19960708
                    Last Updated on STN: 19960708

L20  ANSWER 2 OF 2  DISSABS COPYRIGHT (C) 2006 ProQuest Information and
     Learning Company; All Rights Reserved on STN
ACCESSION NUMBER:   95:14070  DISSABS   Order Number: AARC391489 (not available
                    for sale by UMI)
TITLE:              ENDOGENOUS CHOLECYSTOKININ MODULATES GASTRIC
                    EMPTYING AND POSTPRANDIAL RELEASE OF INSULIN IN HUMANS
                    INFLUENCIA DE LA COLECISTOKININA ENDOGENA EN EL VACIAMIENTO
                    GASTRICO Y EN LA SECRECION POSPRANDIAL DE INSULINA EN EL
```

HOMBRE
AUTHOR: HIDALGO GRAU, LUIS ANTONIO
CORPORATE SOURCE: UNIVERSITAT AUTONOMA DE BARCELONA (SPAIN) (5852)
SOURCE: Dissertation Abstracts International, (1993) Vol. 56, No. 1C, p. 157. Order No.: AARC391489 (not available for sale by UMI). SERVEI DE PUBLICACIONS DE LA UNIVERSITAT AUTONOMA DE BARCELONA, EDIFICI RECTORAT, APARTAT POSTAL 20, E-08193 BELLATERRA (BARCELONA), SPAIN.
ISBN: 84-7929-812-X.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: Spanish
ENTRY DATE: Entered STN: 19950321
Last Updated on STN: 19950321

=> d kwic 1-2

L20 ANSWER 1 OF 2 DISSABS COPYRIGHT (C) 2006 ProQuest Information and Learning Company; All Rights Reserved on STN
AB . . . of radioisotopes for physiological studies....Their use for the labelling of small compounds such as drugs has not been reported.
Cholecystokinin (CCK) is a hormone whose actions have been associated with satiety, and whose levels have been found to be abnormal. . . $\sp{111}$In or $\rm \sp{99m}$Tc using polyaminopolycarboxylic acid chelators is reported. The synthesis of disubstituted as opposed to monosubstituted EDTA and DTPA resulted from reaction of a model amine with the dianhydrides of EDTA and DTPA under various reaction conditions.

L20 ANSWER 2 OF 2 DISSABS COPYRIGHT (C) 2006 ProQuest Information and Learning Company; All Rights Reserved on STN
TI ENDOGENOUS CHOLECYSTOKININ MODULATES GASTRIC EMPTYING AND POSTPRANDIAL RELEASE OF INSULIN IN HUMANS
INFLUENCIA DE LA COLECISTOKININA ENDOGENA EN EL VACIAMIENTO GASTRICO Y.

AB Aim of the study. To determine the effect of endogenous cholecystokinin (CCK) on gastric emptying and postprandial release of insulin in humans.
Materials and method. Six healthy volunteers underwent three experiments.. . . liquid meal containing 100 g glucose, and an egg yolk mixed with 150 ml of milk. To evaluate gastric emptying, Tc99-DTPA (2 mCu) was added to the meal. To evaluate gallbladder emptying, Tc99-HIDA (5 mCu) was given i.v. one hour before. . .

=> s metal chelat?
34727 METAL
11101 METALS
40243 METAL
(METAL OR METALS)
4454 CHELAT?
L21 497 METAL CHELAT?
(METAL(W)CHELAT?)

=> d his

(FILE 'HOME' ENTERED AT 13:35:48 ON 07 DEC 2006)

FILE 'REGISTRY' ENTERED AT 13:36:14 ON 07 DEC 2006
L1 136 S DY'NLE'GW'NLE'DF/SQSP
L2 424 S DYMGWMDF/SQSP

FILE 'CAPLUS' ENTERED AT 13:39:00 ON 07 DEC 2006
L3 84 S L1

```
L4             0 S DPTA AND L3
L5             5 S DOTA AND L3
L6        134722 S CHELAT?
L7            12 S L6 AND L3
L8             0 S L7 NOT PY>1997
L9             1 S L7 NOT PY>1998
L10         4485 S L2
L11           49 S L10 AND L6
L12           20 S L11 NOT PY>1997
L13           20 S L11 NOT PY>1996
L14        14458 S METAL CHELAT?
L15            3 S L14 AND L10
L16            4 S L10 AND (DPTA OR DOTA)
L17            9 S L10 AND DTPA

     FILE 'DISSABS' ENTERED AT 13:46:43 ON 07 DEC 2006
L18          323 S CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK () 8))
L19          360 S DTPA OR DOTA
L20            2 S L19 AND L18
L21          497 S METAL CHELAT?

=> s l21 and l18
L22            0 L21 AND L18

=> file pctfull
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     7.67     136.00

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -3.00

FILE 'PCTFULL' ENTERED AT 13:50:53 ON 07 DEC 2006
COPYRIGHT (C) 2006 Univentio

FILE LAST UPDATED:          5 DEC 2006      <20061205/UP>
MOST RECENT UPDATE WEEK:       200648        <200648/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.
    SEE
    http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE
    (last updated April 10, 2006) <<<

=> s cholecystokinin or (CCK-8 or CCK8 or (CCK () 8))
          1899 CHOLECYSTOKININ
           132 CHOLECYSTOKININS
          1949 CHOLECYSTOKININ
                 (CHOLECYSTOKININ OR CHOLECYSTOKININS)
          2003 CCK
            36 CCKS
          2007 CCK
                 (CCK OR CCKS)
       1002744 8
           255 CCK-8
                 (CCK(W)8)
            63 CCK8
          2003 CCK
            36 CCKS
          2007 CCK
```

```
                (CCK OR CCKS)
        1002744 8
            255 CCK (W) 8
L23        2006 CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK (W) 8))

=> s DPTA or DOTA
            910 DPTA
              1 DPTAS
            910 DPTA
                  (DPTA OR DPTAS)
           1767 DOTA
              5 DOTAS
           1768 DOTA
                  (DOTA OR DOTAS)
L24        2224 DPTA OR DOTA

=> s DTPA or DOTA
           5576 DTPA
             12 DTPAS
           5579 DTPA
                  (DTPA OR DTPAS)
           1767 DOTA
              5 DOTAS
           1768 DOTA
                  (DOTA OR DOTAS)
L25        6121 DTPA OR DOTA

=> s l25 and l23
L26         110 L25 AND L23

=> s l26 not py>1996
         935225 PY>1996
L27          10 L26 NOT PY>1996

=> d ibib 1-10

L27    ANSWER 1 OF 10    PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:       2001076631 PCTFULL
       no bibliographic data available - please use FPI for PI information
DESIGNATED STATES

L27    ANSWER 2 OF 10    PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:       1996040293 PCTFULL  ED 20020514
TITLE (ENGLISH):        STRUCTURALLY DETERMINED METALLO-CONSTRUCTS AND
                        APPLICATIONS
TITLE (FRENCH):         METALLO-ASSEMBLAGES DETERMINES STRUCTURALEMENT ET
                        APPLICATIONS
INVENTOR(S):            SHARMA, Shubh, D.
PATENT ASSIGNEE(S):     RHOMED INCORPORATED;
                        SHARMA, Shubh, D.
LANGUAGE OF PUBL.:      English
DOCUMENT TYPE:          Patent
PATENT INFORMATION:
                        NUMBER              KIND     DATE
                        ---------------------------------
                        WO 9640293            A1 19961219
DESIGNATED STATES
       W:               AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI
                        GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD
                        MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM
                        TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ
                        MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC
                        NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.:      WO 1996-US9840        A  19960606
PRIORITY INFO.:         US 1995-8/476,652        19950607
```

US 1996-8/660,697 19960605

L27 ANSWER 3 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1996039128 PCTFULL ED 20020514
TITLE (ENGLISH): PROTEIN PARTICLES FOR THERAPEUTIC AND DIAGNOSTIC USE
TITLE (FRENCH): PARTICULES PROTEIQUES A USAGE THERAPEUTIQUE ET DIAGNOSTIQUE
INVENTOR(S): YEN, Richard, C., K.
PATENT ASSIGNEE(S): HEMOSPHERE, INC.;
YEN, Richard, C., K.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9639128	A1	19961212

DESIGNATED STATES
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1996-US9458	A	19960604
PRIORITY INFO.:	US 1995-8/471,650		19950606
	US 1995-8/554,919		19951109

L27 ANSWER 4 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995015118 PCTFULL ED 20020514
TITLE (ENGLISH): GAS MICROSPHERES FOR TOPICAL AND SUBCUTANEOUS APPLICATION
TITLE (FRENCH): MICROSPHERES GAZEUSES POUR APPLICATION TOPIQUE ET SOUS-CUTANEE
INVENTOR(S): UNGER, Evan, C.;
MATSUNAGA, Terry;
YELLOWHAIR, David
PATENT ASSIGNEE(S): UNGER, Evan, C.;
MATSUNAGA, Terry;
YELLOWHAIR, David
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9515118	A1	19950608

DESIGNATED STATES
W: AU CA CN JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.:	WO 1994-US13817	A	19941130
PRIORITY INFO.:	US 1993-8/159,674		19931130
	US 1993-8/159,687		19931130
	US 1993-8/160,232		19931130
	US 1994-8/307,305		19940916
	US 1994-8/346,426		19941129

L27 ANSWER 5 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995005842 PCTFULL ED 20020514
TITLE (ENGLISH): METHOD AND DEVICE FOR TREATING GASTROINTESTINAL MUSCLE DISORDERS AND OTHER SMOOTH MUSCLE DYSFUNCTION
TITLE (FRENCH): PROCEDE ET DISPOSITIF POUR TRAITER LES TROUBLES MUSCULAIRES GASTRO-INTESTINAUX ET AUTRES DYSFONCTIONNEMENTS DES MUSCLES LISSES
INVENTOR(S): PASRICHA, Pankaj, J.;
KALLOO, Anthony, N.
PATENT ASSIGNEE(S): THE JOHNS HOPKINS UNIVERSITY

DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9505842	A1	19950302

DESIGNATED STATES
W: CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1994-US9759 A 19940823
PRIORITY INFO.: US 1993-112,088 19930826

L27 ANSWER 6 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1994004674 PCTFULL ED 20020513
TITLE (ENGLISH): HUMAN MELANOCYTE STIMULATING HORMONE RECEPTOR
TITLE (FRENCH): RECEPTEUR D'HORMONE STIMULANT LE MELANOCYTE CHEZ L'HOMME
INVENTOR(S): WIKBERG, Jarl;
CHHAJLANI, Vijay
PATENT ASSIGNEE(S): WIKBERG, Jarl;
CHHAJLANI, Vijay
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9404674	A1	19940303

DESIGNATED STATES
W: AU BB BG BR BY CA CZ FI HU JP KP KR KZ LK MG MN MW NO NZ PL RO RU SD SK UA US VN AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.: WO 1993-DK273 A 19930820
PRIORITY INFO.: DK 1992-1046/92 19920821
DK 1992-1118/92 19920910
DK 1993-528/93 19930505

L27 ANSWER 7 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1993018797 PCTFULL ED 20020513
TITLE (ENGLISH): METHOD OF INTRAOPERATIVELY DETECTING AND LOCATING TUMORAL TISSUES
TITLE (FRENCH): PROCEDE POUR DETECTER ET LOCALISER DE FACON PEROPERATOIRE DES TISSUS TUMORAUX
INVENTOR(S): ENSING, Geert, Jacob;
PANEK, Karel, Jan;
DOEDENS, Bareld, Jan
PATENT ASSIGNEE(S): MALLINCKRODT MEDICAL, INC.;
ENSING, Geert, Jacob;
PANEK, Karel, Jan;
DOEDENS, Bareld, Jan
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9318797	A1	19930930

DESIGNATED STATES
W: AU CA JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1993-US2772 A 19930324
PRIORITY INFO.: NL 1992-92200848.7 19920325

L27 ANSWER 8 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1992004916 PCTFULL ED 20020513
TITLE (ENGLISH): PARTICULATE AGENTS
TITLE (FRENCH): AGENTS SOUS FORME DE PARTICULES
INVENTOR(S): FILLER, Aaron, Gershon

PATENT ASSIGNEE(S): ST. GEORGE'S ENTERPRISES LIMITED;
FILLER, Aaron, Gershon

LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9204916	A2	19920402

DESIGNATED STATES
W: AT AU BE CA CH DE DK ES FR GB GR IT JP LU NL NO SE US

APPLICATION INFO.:	WO 1991-EP1780	A	19910913
PRIORITY INFO.:	GB 1990-9020075.9		19900914
	GB 1990-9023580.5		19901030
	GB 1990-9027293.1		19901217
	GB 1991-9100233.7		19910107
	GB 1991-9100981.1		19910116
	GB 1991-9102146.9		19910131
	GB 1991-9110876.1		19910520
	GB 1991-9116373.3		19910730
	GB 1991-9117851.7		19910819
	GB 1991-9118676.7		19910830

L27 ANSWER 9 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1992001469 PCTFULL ED 20020513
TITLE (ENGLISH): A COMPOSITION PROVIDING IMPROVED CLEARANCE OF BIOACTIVE SUBSTANCES FROM THE BLOODSTREAM
TITLE (FRENCH): COMPOSITION ASSURANT UNE MEILLEURE ELIMINATION DE SUBSTANCES BIOACTIVES CONTENUES DANS LE SYSTEME SANGUIN
INVENTOR(S): SELMER, Johan
PATENT ASSIGNEE(S): NOVO NORDISK A/S;
SELMER, Johan
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9201469	A1	19920206

DESIGNATED STATES
W: AT AU BE CA CH CS DE DK ES FI FR GB GR HU IT JP KR LU NL NO PL SE SU US

APPLICATION INFO.:	WO 1991-DK215	A	19910724
PRIORITY INFO.:	DK 1990-1762/90		19900724

L27 ANSWER 10 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1989009625 PCTFULL ED 20020513
TITLE (ENGLISH): CONTRAST AGENTS FOR MAGNETIC RESONANCE IMAGING
TITLE (FRENCH): AMELIORATIONS APPORTEES A L'IMAGERIE PAR RESONANCE MAGNETIQUE
INVENTOR(S): BERG, Arne;
KLAVENESS, Jo
PATENT ASSIGNEE(S): COCKBAIN, Julian, Roderick, Michaelson;
NYCOMED AS;
BERG, Arne;
KLAVENESS, Jo
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 8909625	A1	19891019

DESIGNATED STATES
W: AT AU BE CH DE DK FI FR GB IT JP LU NL NO SE US

APPLICATION INFO.:	WO 1989-EP376	A	19890406
PRIORITY INFO.:	GB 1988-8808305.0		19880408

=> d kwic 10

L27 ANSWER 10 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . use of paramagnetic
metal chelates, for example of aminopolycarboxylic
acids such as nitrilotriacetic acid (NTA)j]NrNrN1rN'-
ethylenediaminetetraacetic acid (EDTA), N-hydroxyethyl-
-N,N1,N1-ethylenediaminetriacetic acid (HEDTA)r NrNrN'r-
N'',N''-diethylenetriaminepentaacetic acid (DTPA),
and 1,4,7,10-tetraazacyclododecanetetraacetic acid
(DOTA) (see for example EP-A-71564, EP-A-130934t
DE-A-3401052 and US-A-4639365). and Nycomed AS have
suggested the use of paramagnetic metal chelates
of iminodiacetic acids (see. . .

Intravenous administration, at separate timesf of
the positive contrast agent Gd DTPA-dimeglumine (which
following such administration rapidly distributes
extracellularly) and of superparamagnetic ferrite
particles was proposed by Weissleder et al.'in AJR
150: 561-566 (1988) for imaging. . .

. . .
the reticuloendothelial system targetting
negative contrast agents of W085/04330. However,,
extracellularly distributing paramagnetic metal containing
positive contrast agents, such as Gd DTPAF Gd DOTA
and Od DTPA-BMA (the gadolinium chelate of the bismethylamide
of DTPA), may be used according to the present invention
for administration into body cavities or tracts having
externally voiding ducts, e.g. for oral. . .

. . .
metal
chelates in which the paramagnetic metal species
+ 3+ especially Dy 3+ are particularly
is Tb or Sm or more
preferred, eag, Dy DTPA-BMAr, or DyDTPA-beta-alanine-
dextran (molecular weight 70000) where a blood pooling
positive contrast agent is desired.

EDTA; DTPA-BMA; DOTA; desferrioxamine; and the
physiologically
acceptable salts thereof.

. . .
contrast agent,
if uniform distribution after i.v. administration
is desired, one may conveniently use as the chelating
moiety a hydrophilic extracellular substance, such
as DTPA or DOTA or a chelating agent as claimed in
W089/00557. However, to achieve tissue- or duct-
specificity, for either positive or negative MRI
contrast agents. . .

. . .
the same equipment against
distilled water to a volume of 1150 ml, the pH-
was adjusted to 9 with N-methylmorpholine and 29.18g
of DTPA-bis-anhydride was added while the pH was
kept at 8 using the same base. When the solution
became clear, the reaction mixture was. . .

Gd 4.6%; N 2.15%; Na 0.16%; Cl less than 0101%,
1
Free Gd (xylene orange titration), DTPA, GdDTPA?
citric acid, or DMSO (HPLC): less than 0.01%

(The percentages in the analysis results are by weight).

in three of the dogs to which the positive and negative contrast agents were administered, 1.0 unit/kg bodyweight of cholecystokinin were given intravenously 60 minutes after administration of the paramagnetic contrast agent immediately followed by examinations in the transverse and frontal projections.

. . .

gall bladder was also encountered 15 to 30 minutes after contrast agent administration. After administration of the superparamagnetic and paramagnetic contrast agents and after cholecystokinin injection, the gall bladder was moderately contracted and visualization of the choledocus duct was achieved as well as contrast filling of the duodenum.

=> d ibib kwic 1-9

L27 ANSWER 1 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001076631 PCTFULL
no bibliographic data available - please use FPI for PI information
DESIGNATED STATES

DETD 37(4):449-57 [1997]; McHugh, PR. and Moran, TH., The stomach, cholecystokinin, and satiety, Fed. Proc. 45(5):13 84-90 [1986]; Lin, H.C. et al., Frequency ofgastric pacesetter potential depends on volume and site of distension,. . .

There may also be some interactions between 5-HT receptor-mediated effects and cholecystokinin-mediated effects on satiety. (Voight, J.P. et al., Evidencefor the involvement of the 5-HTIA receptor in CKK induced satiety in rats, Nauyn Schmiedebergs Arch. Pharmacol. 351(3):217-20 [1995]; Varga, G. et al., Effect of deramciclane, a new 5-HT receptor antagonist, on cholecystokinin -induced changes in ratgastrointesfinalfunction, Eur. J. Pharrnacol. 367(2-3):315-23 [1999]; but see, Eberle-Wang, K. and Simansky, K.J., Yhe CKK-A receptor antagonist, devazepide, blocks. . .

2 o Behav. 43(3):943-47 [1992]). The neuropeptide hormone cholecystokinin is known to induce satiety, inhibit gastric emptying, and to stimulate digestive pancreatic and gall bladder activity. (Blevins, J.E. et al., Brain regions where cholecystokinin suppresses feeding in rats, Brain Res. 860(1-2):1-10 [2000]; Moran, TH. and McHugh, P.R., Cholecystokinin suppressesfood intake by inhibiting gastric emptying, Am. J. Physiol.

Cholecystokinin, and other neuropeptides, such as bombesin, arnylin, proopiomelanocortin, corticoptropin-releasing factor, galanin, melanin-concentrating hormone, neurotensin, agouti-related protein, leptin, and neuropeptide Y, are important 3. . .

. . .
(preferred dose range of 0 5 mg/kg), deramciclane (Varga, G. et al., Effect of deramciclane, a new 5-HT receptor antagonist, on cholecystokinin-
1 0 induced changes in rat gastrointestinalfunction, Eur. J. Pharmacol. 367(2-3):315-23
(1999]), or alosetron. 5-HT4 receptor antagonists are preferably used at a. . .
. . .
0 with phosphate buffer, pH 7.0, at 2 mL/min. 60 minutes after the start of the perfusion,
5 1
-20 (Xi of Tc-DTPA (diethylenetlianiinepentaacetic acid) was delivered as a bolus into
the test segment. Intestinal transit was then measured by counting the radioactivity of. . .
. . .
liquid marker across the approximately 150 cm intestinal test segment by delivering
about 20 gCi 'Tc chelated to diethyltriamine pentaacetic acid (DTPA)(Cunningham,
K.M. et al., Use of technicium-99m (V)thiocyanate to measure gastric emptying offat,
J. Nucl. Med. 32:878-881 [1991]) as a bolus into the. . . gamma well counter. After correcting
all counts to time zero, intestinal transit was calculated as the cumulative percent recovery
of the delivered Tc-DTPA. This method has been well validated over the years and
appreciated for its advantage of minimal inadvertent marker loss. To demonstrate. . .

L27 ANSWER 2 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1996040293 PCTFULL ED 20020514
TITLE (ENGLISH): STRUCTURALLY DETERMINED METALLO-CONSTRUCTS AND APPLICATIONS
TITLE (FRENCH): METALLO-ASSEMBLAGES DETERMINES STRUCTURALEMENT ET APPLICATIONS
INVENTOR(S): SHARMA, Shubh, D.
PATENT ASSIGNEE(S): RHOMED INCORPORATED;
SHARMA, Shubh, D.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9640293	A1	19961219

DESIGNATED STATES
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1996-US9840	A	19960606
PRIORITY INFO.:	US 1995-8/476,652		19950607
	US 1996-8/660,697		19960605

DETD . . . or Cu., to an equirnolar covalent
adduct of diethylenetriaminepentaacetic acid (DT?A) with ethylenediamine. This adduct
may be achieved by reacting ethylenediamine with DTPA
-dianhydride. The amino group
of the ethylenediamine moiety in this adduct, together with the free carboxylate of the DTPA

moiety, mimic the two primary integrin receptor-binding functionalities. The use of higher
hornologues of ethylenediarnine, or use of other di-amines, such as. . .
. . .
a reversed turn structure as their hypothesized biologically active structure. The
exan3ples of these include various peptide hormones such as somatostatin, cholecystokinin,
opioid peptides, melanotropins, luteinizing hormone releasing hormone, tachykinins and
various antibody epitopes.

L27 ANSWER 3 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1996039128 PCTFULL ED 20020514
TITLE (ENGLISH): PROTEIN PARTICLES FOR THERAPEUTIC AND DIAGNOSTIC USE
TITLE (FRENCH): PARTICULES PROTEIQUES A USAGE THERAPEUTIQUE ET DIAGNOSTIQUE
INVENTOR(S): YEN, Richard, C., K.
PATENT ASSIGNEE(S): HEMOSPHERE, INC.;
YEN, Richard, C., K.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9639128	A1	19961212

DESIGNATED STATES
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1996-US9458	A	19960604
PRIORITY INFO.:	US 1995-8/471,650		19950606
	US 1995-8/554,919		19951109

DETD . . . factor beta
receptor
14. anti-beta-lipoprotein
15. alpha 2-macroglobulin
16. streptokinase
17. anti-progesterone antibody
18. anti-leukotriene B4 antibody
19. CGGRGDF-NH2
20. doxorubicin
21. daunarubicin
22. EDTA-conjugated to HSA
23. DTPA-conjugated to HSA
24. technetium
25. gadolinium
26. HSA conjugated to FITC (Fluorescein Isothiocyanate)
27. HSA conjugated to TRITC (Tetramethylrhodamine B isothiocyanate)
28. HSA conjugated to. . . Tc99m can be achieved through direct covalent bonding or through a chelating agent. Examples of chelating agents are cysteine-cyclohexanol conjugate and DTPA

Biologically active peptides:
myl-L-Ala-D-Glu Amide
N-Acetyl-Asp-Glu
42

N-Acetyl-Cholecystokinin and its fragments
N-Acetyl-Hirudin and its fragments
Acetyl-Leu-Leu-Argininal
N-Acetyl-Leu-Leu-Methioninal
N-Acetyl-Leu-Leu-Norleucinal
Acetyl-Met-Asp-Arg-Val-Leu-Ser-Arg-Tyr
N-Acetyl-Met-Leu-Phe
N-Acetylmuramyl-D-alanyl-D-isoglutamine
N-Acetylmuramyl-L-alanyl-D-isoglutamine
N-Acetylmuramyl-L-alanyl-L-isoglutamine
N-Acetylmuramyl-Ala-D-isoglutaminyl-Ne-stearoyl-Lys
N-Acetyl-Phe-Nle-Arg-Phe Amide
Acetyl-Renin Substrate Tetradecapeptide
Acetyl-Ser-Asp-Lys-Pro
Acetyl-Ser-Gln-Asn-Tyr
Acetyl-Ser-Gln-Asn-Tyr-Pro-Val-Val Amide. . .
Carassin
N-Carboxymethyl-Phe-Leu
Cardioexcitatory Peptide
45
alpha-Casein and fragments
Beta-Casomorphin
Na-CBZ-Arg-Arg-Pro-Phe-His-Sta-Ile-His-Ne-BOC-Lys Methyl Ester
1 Ester
CBZ-Leu-Val-Gly Diazomethyl Ketone
N-CBZ-D-Phe-Phe-Gly
N-CBZ-Pro-D-Leu
N-CBZ-Pro-Leu-Gly Hydroxamate
CD4 and fragments
Cecropins
Cerebellin
Chemostactic Peptides
Cholecystokinin and fragments
Chorionic Gonadotropin and fragments
Chromostatin-20
Chymostatin
Circumsporozoite (CS) Protein of Plasmodium falciparum
repetitive sequences
Collagen
Conotoxin GI
A-conotoxin GIIIB
w-conotoxin GVIA
a-conotoxin SI
Copper. . .
.
NITR7, DM-nitrophen, NITRS/AM; Ammonium N-
nitrosophenyl-hydroxylamine; Ammonium purpurate;
alpha-Benzoin oxime; N, N-Bis-(hydroxyethyl)-glycine;
2,3-butane-dione dioxime; Trans-1,2-Diaminocyclo-
hexanetetra-acetic acid (CDTA); Diethylene-
triaminopenta-acetic acid (DTPA); 4,5-Dihydroxy-
benzene-1,3-disulphonic acid; 2,3-Dimercapto-1-
60
Propanol; Diphenylthio-carbazone; 2,2'-Dipyridyl;
3,6-Disulpho-1,8-dihydroxy-naphthalene;
Dithiooxamide; Eriochrome Black T; Ethylene-diamine;
Ethylenediaminetetraacetic acid (EDTA); (Ethylene-
dioxy)-diethylenedinitrilo-tetraacetic acid (EGTA);
o-Hydroxybenzaldehyde. . .

L27 ANSWER 4 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995015118 PCTFULL ED 20020514
TITLE (ENGLISH): GAS MICROSPHERES FOR TOPICAL AND SUBCUTANEOUS APPLICATION
TITLE (FRENCH): MICROSPHERES GAZEUSES POUR APPLICATION TOPIQUE ET

SOUS-CUTANEE

INVENTOR(S): UNGER, Evan, C.;
MATSUNAGA, Terry;
YELLOWHAIR, David

PATENT ASSIGNEE(S): UNGER, Evan, C.;
MATSUNAGA, Terry;
YELLOWHAIR, David

LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9515118	A1	19950608

DESIGNATED STATES
W: AU CA CN JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.:	WO 1994-US13817	A	19941130
PRIORITY INFO.:	US 1993-8/159,674		19931130
	US 1993-8/159,687		19931130
	US 1993-8/160,232		19931130
	US 1994-8/307,305		19940916
	US 1994-8/346,426		19941129

DETD . . . of topical or subcutaneous application and delivery: melanin concentrating hormone,, melanin stimulating hormone, trypsin inhibitor, Bowman Burk inhibitor, luteinizing hormone releasing hormone (LHRH), bombesin, cholecystokinin, insulin, gastrin, endorphins, enkephalins, growth hormone, prolactin, oxytocin, follicle stimulating hormone (FSH), human chorionic gonadotropin,, corticotropin, 0 and lipotropin, calcitonin, glucagon, thyrotropin, elastin, cyclosporin,. . .

Suitable chelants and chelating agents include, but are not limited to: penicillamine; citrate; ascorbate; diethylenetriaminepentaacetic acid (DTPA), and derivatives and salts thereof; dihydroxypropylethylenediamine (DPEA), and derivatives and salts thereof; cyclohexanediaminetetraacetic acid (CHTA), and derivatives and salts thereof; ethylenediaminetetraacetic acid (EDTA), and. . . thereof; N,Nf-(1,2-ethanedivinylbis(oxy-2,1-phenylene))bis(N-(carboxymethyl) (BAPTA), and derivatives and salts thereof; aminophenol-triacetic acid (APTRA), and derivatives and salts thereof; tetrakis(2-pyridylmethyl)ethylenediamine (TPEN), and derivatives and salts thereof; 1.4,7,10-tetraazacyclodecane (DOTA) and derivatives and salts thereof; and cyanins and their derivatives,
Furthermore, immunosuppressants or anti-inflammatory preparations can be incorporated into the gas and gaseous. . .

These metal ions may be incorporated into the microspheres as free salts, as complexes, e,g., with EDTA, DTPA, DOTA or
desferrioxamine, or as oxides of the metal ions,
Additionally, derivatized complexes of the metal ions may be bound to lipid head groups,. . .

CLMEN. . . peptides selected from the group consisting of melanin concentrating hormone, melanin stimulating hormone, trypsin inhibitor, Bowman Burk inhibitor, luteinizing hormone releasing hormone, bombesin, cholecystokinin, insulin, gastrin, endorphins, enkephalins, growth hormone, prolactin, oxytocin, follicle stimulating hormone, human chorionic gonadotropin, corticotropin, 0-lipotropin, 7-lipotropin,

calcitonin, glucagon, thyrotropin, elastin, cyclosporin, and collagen, and. . .

. . .

peptides selected from the group consisting of melanin concentrating hormone, melanin stimulating hormone, trypsin inhibitor, Bowman Burk inhibitor, luteinizing hormone releasing hormone, bombesin, cholecystokinin, insulin, 10 gastrin,, endorphins, enkephalins, growth hormone, prolactin, oxytocin, follicle stimulating hormone, human chorionic gonadotropin, corticotropin, fl-lipotropin, T-lipotropin, calcitonin, glucagon, thyrotropin, elastin, cyclosporin, and collagen,. . .

L27 ANSWER 5 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995005842 PCTFULL ED 20020514
TITLE (ENGLISH): METHOD AND DEVICE FOR TREATING GASTROINTESTINAL MUSCLE DISORDERS AND OTHER SMOOTH MUSCLE DYSFUNCTION
TITLE (FRENCH): PROCEDE ET DISPOSITIF POUR TRAITER LES TROUBLES MUSCULAIRES GASTRO-INTESTINAUX ET AUTRES DYSFONCTIONNEMENTS DES MUSCLES LISSES
INVENTOR(S): PASRICHA, Pankaj, J.; KALLOO, Anthony, N.
PATENT ASSIGNEE(S): THE JOHNS HOPKINS UNIVERSITY
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9505842	A1	19950302

DESIGNATED STATES
W: CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1994-US9759 A 19940823
PRIORITY INFO.: US 1993-112,088 19930826

DETD Figs. 3A and B show the effect of intrasphincteric injection of BoTx on LES response to cholecystokinin octapeptide (CCK)

. . .

0.01). The response of the LES to the IV administration of edrophonium (Tensilon; ICN Pharmaceuticals Inc., Costa Mesa, CA) and cholecystokinin
octapeptide (CCK-8) (Kinevac; ER Squibb amp;Sons, Princeton, NJ) in three
additional piglets was also measured. LES pressures, measured by a DENTSLEEVE, were. . .

. . .

retention studies
After an overnight fast, patients were asked to ingest a corn-flake meal with milk containing 0.531 mci 99 aiTc DTPA. Subsequently, serial dynamic
images were obtained with the subject sitting erect in front of a gamma camera.
Retention was expressed. . .

L27 ANSWER 6 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1994004674 PCTFULL ED 20020513
TITLE (ENGLISH): HUMAN MELANOCYTE STIMULATING HORMONE RECEPTOR
TITLE (FRENCH): RECEPTEUR D'HORMONE STIMULANT LE MELANOCYTE CHEZ L'HOMME
INVENTOR(S): WIKBERG, Jarl; CHHAJLANI, Vijay
PATENT ASSIGNEE(S): WIKBERG, Jarl; CHHAJLANI, Vijay
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE

	WO 9404674	A1	19940303
DESIGNATED STATES W:	AU BB BG BR BY CA CZ FI HU JP KP KR KZ LK MG MN MW NO NZ PL RO RU SD SK UA US VN AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG		
APPLICATION INFO.:	WO 1993-DK273	A	19930820
PRIORITY INFO.:	DK 1992-1046/92		19920821
	DK 1992-1118/92		19920910
	DK 1993-528/93		19930505

DETD . . . the substance P receptor, substance K receptor, endothelin receptor, angiotensin receptor, chemoattractant peptide receptor, bombesin receptor, oxytocin receptor, vasopressin receptor, antidiuretic hormone receptor, gastrin receptor, cholecystokinin receptor, canabinoid receptor, follicle stimulating hormone receptor, luteinizing hormone receptor, growth hormone receptor, thyrotropin receptor,, calcitonin receptor, calcitonin gene related peptide receptor and/or parathyroid. . .

isothiocyanatobenzyl EDTA (CITC), diethylenetriaminepenta-acetic acid (DTPA) and be coupled via the mixed anhydride or the cyclic anhydride (Hnatowich 1990). However, since such complexes may provide somewhat unstable chelation and more-over during their manufacture intra and intermolecular cross linking of antibodies, other chelators such as e.g. GYK-DTPA or SCN-Bz-DTPA may be used as an alternative (Hnatowich 1990). Radiolabelling of 99mTc to the antibody may be afforded by using direct labelling techniques. . .

L27 ANSWER 7 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER:	1993018797 PCTFULL ED 20020513
TITLE (ENGLISH):	METHOD OF INTRAOPERATIVELY DETECTING AND LOCATING TUMORAL TISSUES
TITLE (FRENCH):	PROCEDE POUR DETECTER ET LOCALISER DE FACON PEROPERATOIRE DES TISSUS TUMORAUX
INVENTOR(S):	ENSING, Geert, Jacob; PANEK, Karel, Jan; DOEDENS, Bareld, Jan
PATENT ASSIGNEE(S):	MALLINCKRODT MEDICAL, INC.; ENSING, Geert, Jacob; PANEK, Karel, Jan; DOEDENS, Bareld, Jan
LANGUAGE OF PUBL.:	English
DOCUMENT TYPE:	Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9318797	A1	19930930
DESIGNATED STATES W: AU CA JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE		
APPLICATION INFO.: WO 1993-US2772	A	19930324
PRIORITY INFO.: NL 1992-92200848.7		19920325

DETD . . . thyroid-stimulating hormone, vasoactive intestinal polypeptide, prolactin, thyrotropin-releasing hormone, insulin, adrenocorticotropic hormone (ACTH), in particular o(--MSH (melanocyte-stimulating hormone) and f -(methylsulfonyl)-L- c4-aminobutyryl-L-d-glutamyl-L-histidyl-L-

0 phenylaianyl-D-lysyl-L-phenylaianine, cholecystokinin, corticotropin-releasing
hormone (CRH), growth hormone-releasing hormone (GRH), arginine and lysine
vasopressin, oxytocin, glucagon, secretin, parathyroid hormone (PTH) and PTH
related peptide.

bond to an amino group of said
peptide and is derived from ethylene diamine tetra-acetic acid (EDTA), di-
ethylene triamine penta-acetic acid (DTPA),
ethyleneglycol-0,0'-bis(2-
aminoethyl)-N,N,N',N'-tetra-acetic acid (EGTA), N,N-bis(hydroxybenzyl)-
ethylenediamine-N,N'-diacetic acid (HBED), triethylene tetramine hexa-acetic
acid (TTHA), 1,4,7,10-tetraazacyclododecane-N,N',N,N'-tetra-acetic acid
(DOTA), 1 8,11-tetra-azacyclotetradecane-NN',N,N'-tetra-acetic acid
(TETA),, 1 diaminocyclohexane tetra-acetic acid (DCTA), substituted DTPA,
substituted EDTA, or from a compound of the general formula
-R-
S] Y
wherein R is a branched or non-branched, optionally substituted hydrocarbyl
radical,. . .

A, Preparation of DTPA-Octreotide kit
The DTPA-Octreotide kit formulated on basis of sodium acetate buffer with the final composition
3,89 mg sodium acetate
0,029 mg acetic acid
10 gg DTPA-Octreotide
per vial is prepared as follows.

To formulate the kit, 0,5 mg of DTPA-Octreotide is dissolved in 4 ml of acetic acid solution, and 5 ml of sodium acetate solution are added.

In a similar way, starting from 2.5 mg DTPA-Octreotide was also prepared and a kit containing 50gg DTPA-Octreotide per vial.

C, Labelling of DTPA-Octreotide kit with Tb
Several kits of DTPA-Octreotide, prepared according to Example I containing 10 or 50 gg DTPA-Octreotide, are labelled by addition of 0.5 ml of Tb-161 solution obtained under B. The mixture is incubated for 30 min. at room temperature.

ITLC as described above,
Tb DTPA-Octreotide Rf ca 0 0.6
Free Tb-161 Rf ca 0,9 0
Hydrolysed Tb-161 Rf ca 0 0,1
HPLC: Column: gBondapakBC 18 10pn, 3.9 x. . .

>92%
78.4% >93%
challenge experiment with serum (bovine), added at 24 h
76.4% >95%
Free Tb-161 was not detectable in any kit containing 50 gg DTPA-Octreotide.

h - HPLC 96.2%

HPLC identification positive, because UV spectrum and activity peaks of Tb-161 are found identical with those for In-III labelled DTPA-Octreotide used as control.

EXAMPLE 11
Labelling of DTPA-Octreotide kit with Yb-175 and its use in combination with detectincr agent DTPA I-Tvr'-Octreotide
A. Labellincf of DTPA-Octreotide kit with Yb
Ca 1 mg of enriched (97.8%) 174-Yb2O2 is irradiated for 48 hours in a nuclear reactor with thermal. . .

Several kits containing 10 gg of DTPA-Octreotide prepared according to Example I are labelled by addition of I ml of the Yb-175 stock solution. The mixture is let to-incubate 30. . .

Yb-175 Octreotide: LY at 3 ho ITLC Rf 0 06 91,2%
at 24 h. ITLC Rf 0,5-06 91,7%
B, Preiparation of DTPA 125-Tyr3-Octreotide.

DTPA-Tyr3-Octreotide of the formula
DTPA- (D) Phe-Cys -Tyr*- (D) Trp-Lys -Thr-Cys -Throl
is prepared from Tyr3-Octreotide in a corresponding manner as described in Int, Pat, Appln, WO. . . Example 1, and further iodinated with 125I sodium iodide, dissolved in phosphate buffer in the presence of chloramine T. The molar ratio of DTPA-Tyr3-Octreotide; chloramine T: 125-I is 1:4,6:0,6 The reaction is terminated with 10% BSA solution. The labelled product of the above formula wherein Tyr] =. . .

To combine the therapeutical effect with the radioguided surgery are used both preparations; Yb Octreotide for the desired therapeutic effect and DTPA I-Tyr 3_ Octreotide as the detectingu agent,
Depending on the conditions, they can be used separately, in this case by administering Yb Octreotide first to cause partial or deep tumour necrosis, followed by administration of DTPA I-Tyr3-Octreotide to guide the tumours removal, or they can be administered simultaneously as a mixture in an appropriate ratio. Such a mixture. . .

EXAMPLE III
Labelling of DTPA-Octreotide kit with Ho-166 and its use in combination with Octreotide labelled with Tb
A. Labelling of DTPA-Octreotide kit with Ho 6-
Ca 1 mg of natural (monoisotopic) 165-Ho2O3 is irradiated for 48 hours in nuclear reactor with a thermal. . .

Several kits, containing lOgg of DTPA-Octreotide prepared according to Example I., are labelled by addition of 0.5 or 1 ml of Ho-166 stock solution. The mixture is let. . .

Labelled Ho Octreotide 9111%
Free Ho-166 8,9%
B. Pre-oaration of DTPA-Tb Octreotide as described in Example I., with kit containing 50 Ltq DTPA-Octreotide.

CLMEN. . . amide bond to an amino group of said peptide and being derived from ethylene diamine tetra-acetic acid (EDTA), diethylene triamine penta-acetic acid (DTPA), ethyleneglycol-0,01-bis(2-aminoethyl)-N,N,N',N'-tetra-acetic acid (EGTA), N,N.bis(hydroxybenzyl)-

ethylenediamine-N,N'-diacetic acid (HBED), triethylene tetramine hexa-acetic
acid (TTHA), 1,4,7,10-tetraazacyclododecane-N,N,N,Nf-tetra-acetic acid (DOTA),, 1 8,,11-tetra-azacyclotetradecane-N,N',N,N'-tetra-acetic acid
(TETA), 1,2-diaminocyclohexane tetra-acetic acid (DCTA), substituted DTPA,
substituted EDTA, or from a
compound of the general formula
NO
wherein R is a branched or non-branched, optionally substituted hydrocarbyl
radical, which may be. . .

L27 ANSWER 8 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1992004916 PCTFULL ED 20020513
TITLE (ENGLISH): PARTICULATE AGENTS
TITLE (FRENCH): AGENTS SOUS FORME DE PARTICULES
INVENTOR(S): FILLER, Aaron, Gershon
PATENT ASSIGNEE(S): ST. GEORGE'S ENTERPRISES LIMITED;
FILLER, Aaron, Gershon
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9204916	A2	19920402
DESIGNATED STATES W:	AT AU BE CA CH DE DK ES FR GB GR IT JP LU NL NO SE US		
APPLICATION INFO.:	WO 1991-EP1780	A	19910913
PRIORITY INFO.:	GB 1990-9020075.9		19900914
	GB 1990-9023580.5		19901030
	GB 1990-9027293.1		19901217
	GB 1991-9100233.7		19910107
	GB 1991-9100981.1		19910116
	GB 1991-9102146.9		19910131
	GB 1991-9110876.1		19910520
	GB 1991-9116373.3		19910730
	GB 1991-9117851.7		19910819
	GB 1991-9118676.7		19910830

DETD Paramagnetic contrast agents such as gadolinium-DTPA act primarily by altering T, relaxation rates.
. . .
its ease of use as a
histocheiAcal marker. Other studies have demonstrated
transport of a wide variety of substances including
Vasoactive Intestinal Polypeptide (VIP),
cholecystokinin, substance P and somatostatin,
neuropeptide-Y, and adriamycin. These types of tracers
have sometimes been introduced by intravenous injection
with subsequent uptake by neurons. . .

The use of a magnetic resonance small molecule
contrast agent such as gadolinium-DTPA (diethylene-
triaminepentaacetic acid) required the introduction of a
very high concentration into the nerve and this amount
was beyond what could be achieved,. . .

6) A wide variety of peptides and small proteins
such as endorphins, vasoactive intestinal polypeptide,
calcitonin gene-related peptide, cholecystokinin,
substance P, somatostatin, and neuropeptide Y or the
relevant portions of such peptides for the encouragement

of neuronal uptake and transport.

Additional types of agents for imaging include paramagnetic metal chelates of polychelants (e.g. poly-lysine gadolinium-DTPA 40 which uses the macromolecularlparticulate aspects of uptake to introduce groups of paramagnetic nuclei (40 Gd atoms per molecule) (see EP-A-305320, EP-A-357622, EP-A-355097, EP-A-331616,. . .

L27 ANSWER 9 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1992001469 PCTFULL ED 20020513
TITLE (ENGLISH): A COMPOSITION PROVIDING IMPROVED CLEARANCE OF BIOACTIVE SUBSTANCES FROM THE BLOODSTREAM
TITLE (FRENCH): COMPOSITION ASSURANT UNE MEILLEURE ELIMINATION DE SUBSTANCES BIOACTIVES CONTENUES DANS LE SYSTEME SANGUIN
INVENTOR(S): SELMER, Johan
PATENT ASSIGNEE(S): NOVO NORDISK A/S;
SELMER, Johan
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9201469	A1	19920206

DESIGNATED STATES
W: AT AU BE CA CH CS DE DK ES FI FR GB GR HU IT JP KR LU NL NO PL SE SU US
APPLICATION INFO.: WO 1991-DK215 A 19910724
PRIORITY INFO.: DK 1990-1762/90 19900724

DETD . . . radioimaging leukocytes by injecting a conjugate of an antibody reactive with a leukocyt6 surface molecule and a radioisotope chelated with an EDTA or DTPA derivative followed by the injection of an antibody against the conjugate in order to clear the conjugate/antibody complex through the reticuloendothelial system.. . .

. . .
hormone,,;
follicle-Stimulating
hormone,, luteinising
h o r m o n e r
adrenocorticotropic
hormone, parathyroidea
hormone, prolactin,
l i p o t r o p i n J,
cholecystokinin,
calcitonin, secretin,
atrialnatriuretic
factor, endothelin,
vasoactive intestinal
p o l y p e p t i d e r
transferrin, tachykinin
Intercellular adhesion
factors intercellular adhesion
molecule 1, endothelial
leukocyte. . .

=> octapeptide
OCTAPEPTIDE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

```
=> s octapeptide
          1500 OCTAPEPTIDE
           238 OCTAPEPTIDES
L28       1631 OCTAPEPTIDE
                 (OCTAPEPTIDE OR OCTAPEPTIDES)

=> s l28 and (DTPA or DOTA)
          5576 DTPA
            12 DTPAS
          5579 DTPA
                 (DTPA OR DTPAS)
          1767 DOTA
             5 DOTAS
          1768 DOTA
                 (DOTA OR DOTAS)
L29         86 L28 AND (DTPA OR DOTA)

=> s l29 not py>1996
        935225 PY>1996
L30         15 L29 NOT PY>1996

=> s l30 and CCK
          2003 CCK
            36 CCKS
          2007 CCK
                 (CCK OR CCKS)
L31          1 L30 AND CCK

=> d ibib

L31    ANSWER 1 OF 1      PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        1995005842 PCTFULL  ED 20020514
TITLE (ENGLISH):         METHOD AND DEVICE FOR TREATING GASTROINTESTINAL MUSCLE
                         DISORDERS AND OTHER SMOOTH MUSCLE DYSFUNCTION
TITLE (FRENCH):          PROCEDE ET DISPOSITIF POUR TRAITER LES TROUBLES
                         MUSCULAIRES GASTRO-INTESTINAUX ET AUTRES
                         DYSFONCTIONNEMENTS DES MUSCLES LISSES
INVENTOR(S):             PASRICHA, Pankaj, J.;
                         KALLOO, Anthony, N.
PATENT ASSIGNEE(S):      THE JOHNS HOPKINS UNIVERSITY
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
                         ---------------------------------
                         WO 9505842           A1 19950302
DESIGNATED STATES
      W:                 CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.:       WO 1994-US9759       A  19940823
PRIORITY INFO.:          US 1993-112,088         19930826


=> d kwic

L31    ANSWER 1 OF 1      PCTFULL   COPYRIGHT 2006 Univentio on STN

DETD   Figs. 3A and B show the effect of intrasphincteric injection of BoTx on
       LES response to cholecystokinin octapeptide (CCK)
  . . .
       The response of the LES to the IV administration of edrophonium
       (Tensilon; ICN Pharmaceuticals Inc., Costa Mesa, CA) and cholecystokinin
         octapeptide (CCK-8) (Kinevac; ER Squibb amp;Sons,
       Princeton, NJ) in three
       additional piglets was also measured. LES pressures, measured by a
       DENTSLEEVE, were recorded in response to IV edrophonium (5 mg). After a
       SUBSTITUTE SHEET (RULE 26)
```

washout period of 10 minutes, CCK (5 µg IV) was then administered.
Subsequently, BoTx was injected into the LES, as described above, and the
experiment was. . .

Intrasphincteric BoTx also altered the response of the LES to CCK
(Figure 3). In untreated piglets, CCK did not cause any significant change in
LES pressure. However, after intrasphincteric BoTx injection, a significant
increase in LES pressure was seen in response to CCK. It should be noted that
despite what was felt to be an adequate washout period (10 minutes) in between
injections, basal. . .

. . .
retention studies
After an overnight fast, patients were asked to ingest a corn-flake meal
with milk containing 0.531 mci 99 aiTc DTPA. Subsequently, serial dynamic
images were obtained with the subject sitting erect in front of a gamma camera.
Retention was expressed. . .

=> d his

(FILE 'HOME' ENTERED AT 13:35:48 ON 07 DEC 2006)

FILE 'REGISTRY' ENTERED AT 13:36:14 ON 07 DEC 2006
L1 136 S DY'NLE'GW'NLE'DF/SQSP
L2 424 S DYMGWMDF/SQSP

FILE 'CAPLUS' ENTERED AT 13:39:00 ON 07 DEC 2006
L3 84 S L1
L4 0 S DPTA AND L3
L5 5 S DOTA AND L3
L6 134722 S CHELAT?
L7 12 S L6 AND L3
L8 0 S L7 NOT PY>1997
L9 1 S L7 NOT PY>1998
L10 4485 S L2
L11 49 S L10 AND L6
L12 20 S L11 NOT PY>1997
L13 20 S L11 NOT PY>1996
L14 14458 S METAL CHELAT?
L15 3 S L14 AND L10
L16 4 S L10 AND (DPTA OR DOTA)
L17 9 S L10 AND DTPA

FILE 'DISSABS' ENTERED AT 13:46:43 ON 07 DEC 2006
L18 323 S CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK () 8))
L19 360 S DTPA OR DOTA
L20 2 S L19 AND L18
L21 497 S METAL CHELAT?
L22 0 S L21 AND L18

FILE 'PCTFULL' ENTERED AT 13:50:53 ON 07 DEC 2006
L23 2006 S CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK () 8))
L24 2224 S DPTA OR DOTA
L25 6121 S DTPA OR DOTA
L26 110 S L25 AND L23
L27 10 S L26 NOT PY>1996

```
L28         1631 S OCTAPEPTIDE
L29           86 S L28 AND (DTPA OR DOTA)
L30           15 S L29 NOT PY>1996
L31            1 S L30 AND CCK

=> s l23 and chelat?
         44321 CHELAT?
L32        591 L23 AND CHELAT?

=> s l32 and (radio? or imag?)
        190519 RADIO?
        202203 IMAG?
L33        495 L32 AND (RADIO? OR IMAG?)

=> s l33 not py>1996
        935225 PY>1996
L34         34 L33 NOT PY>1996

=> d his

     (FILE 'HOME' ENTERED AT 13:35:48 ON 07 DEC 2006)

     FILE 'REGISTRY' ENTERED AT 13:36:14 ON 07 DEC 2006
L1          136 S DY'NLE'GW'NLE'DF/SQSP
L2          424 S DYMGWMDF/SQSP

     FILE 'CAPLUS' ENTERED AT 13:39:00 ON 07 DEC 2006
L3           84 S L1
L4            0 S DPTA AND L3
L5            5 S DOTA AND L3
L6       134722 S CHELAT?
L7           12 S L6 AND L3
L8            0 S L7 NOT PY>1997
L9            1 S L7 NOT PY>1998
L10        4485 S L2
L11          49 S L10 AND L6
L12          20 S L11 NOT PY>1997
L13          20 S L11 NOT PY>1996
L14       14458 S METAL CHELAT?
L15           3 S L14 AND L10
L16           4 S L10 AND (DPTA OR DOTA)
L17           9 S L10 AND DTPA

     FILE 'DISSABS' ENTERED AT 13:46:43 ON 07 DEC 2006
L18         323 S CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK () 8))
L19         360 S DTPA OR DOTA
L20           2 S L19 AND L18
L21         497 S METAL CHELAT?
L22           0 S L21 AND L18

     FILE 'PCTFULL' ENTERED AT 13:50:53 ON 07 DEC 2006
L23        2006 S CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK () 8))
L24        2224 S DPTA OR DOTA
L25        6121 S DTPA OR DOTA
L26         110 S L25 AND L23
L27          10 S L26 NOT PY>1996
L28        1631 S OCTAPEPTIDE
L29          86 S L28 AND (DTPA OR DOTA)
L30          15 S L29 NOT PY>1996
L31           1 S L30 AND CCK
L32         591 S L23 AND CHELAT?
L33         495 S L32 AND (RADIO? OR IMAG?)
L34          34 S L33 NOT PY>1996

=> s l34 and l28
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L35 8 L34 AND L28

=> d ibib 1-8

L35 ANSWER 1 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1996039161 PCTFULL ED 20020514
TITLE (ENGLISH): MULTI-TYROSINATED SOMATOSTATIN ANALOGS
TITLE (FRENCH): ANALOGUES DE LA SOMATOSTATINE CONTENANT PLUSIEURS DE TYROSINES
INVENTOR(S): COY, David, H.;
WOLTERING, Eugene, A.;
O'DORISIO, M., Sue;
O'DORISIO, Thomas, M.;
MURPHY, William, A.
PATENT ASSIGNEE(S): THE ADMINISTRATORS OF THE TULANE EDUCATIONAL FUND ;
THE OHIO STATE UNIVERSITY RESEARCH FOUNDATION;
THE LOUISIANA STATE UNIVERSITY MEDICAL CENTER FOUNDATION;
CHILDREN'S HOSPITAL, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9639161	A1	19961212

DESIGNATED STATES W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1996-US8437	A	19960603
PRIORITY INFO.:	US 1995-8/462,223		19950605

L35 ANSWER 2 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1994023724 PCTFULL ED 20020513
TITLE (ENGLISH): MEMBRANE-PERMEANT SECOND MESSENGERS
TITLE (FRENCH): MESSAGERS SECONDAIRES S'INFILTRANT DANS LA MEMBRANE CELLULAIRE
INVENTOR(S): TSIEN, Roger, Y.;
SCHULTZ, Carsten
PATENT ASSIGNEE(S): THE REGENTS OF THE UNIVERSITY OF CALIFORNIA
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9423724	A1	19941027

DESIGNATED STATES W: AU BB BG BR BY CA CN CZ FI HU JP KP KR KZ LK LV MG MN MW NO NZ PL RO RU SD SI SK UA UZ VN AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1994-US3889	A	19940408
PRIORITY INFO.:	US 1993-45,585		19930409

L35 ANSWER 3 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1994022444 PCTFULL ED 20020513
TITLE (ENGLISH): TRICYCLIC COMPOUNDS FOR INHIBITING PLATELET AGGREGATION
TITLE (FRENCH): COMPOSES TRICYCLIQUES UTILISES POUR INHIBER L'AGREGATION PLAQUETTAIRE
INVENTOR(S): CALLAHAN, James, Francis;
HUFFMAN, William, F.
PATENT ASSIGNEE(S): SMITHKLINE BEECHAM CORPORATION;

CALLAHAN, James, Francis;
HUFFMAN, William, F.

LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9422444	A1	19941013

DESIGNATED STATES
W: JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1994-US3383 A 19940329
PRIORITY INFO.: US 1993-8/038,382 19930329

L35 ANSWER 4 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1993008842 PCTFULL ED 20020513
TITLE (ENGLISH): HEMOGLOBINS AS DRUG DELIVERY AGENTS
TITLE (FRENCH): HEMOGLOBINES UTILISEES COMME AGENTS ADMINISTRATEURS DE MEDICAMENTS
INVENTOR(S): ANDERSON, David, C.;
MATHEWS, Antony, James
PATENT ASSIGNEE(S): SOMATOGEN, INC.;
ANDERSON, David, C.;
MATHEWS, Antony, James
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9308842	A1	19930513

DESIGNATED STATES
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK LU MG MN MW NL NO PL RO RU SD SE UA US AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE BF BJ CF CG CI CM GA GN ML MR SN TD TG
APPLICATION INFO.: WO 1992-US9713 A 19921106
PRIORITY INFO.: US 1991-789,177 19911108
US 1991-789,179 19911108

L35 ANSWER 5 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1993000095 PCTFULL ED 20020513
TITLE (ENGLISH): BICYCLIC FIBRINOGEN ANTAGONISTS
TITLE (FRENCH): ANTAGONISTES BICYCLIQUES DE FIBRINOGENE
INVENTOR(S): BONDINELL, William, Edward;
CALLAHAN, James, Francis;
HUFFMAN, William, Francis;
KEENAN, Richard, McCulloch;
KU, Thomas, Wen-Fu;
NEWLANDER, Kenneth, Allen
PATENT ASSIGNEE(S): SMITHKLINE BEECHAM CORPORATION;
BONDINELL, William, Edward;
CALLAHAN, James, Francis;
HUFFMAN, William, Francis;
KEENAN, Richard, McCulloch;
KU, Thomas, Wen-Fu;
NEWLANDER, Kenneth, Allen
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9300095	A2	19930107

DESIGNATED STATES
W: AU CA JP KR US AT BE CH DE DK ES FR GB GR IT LU MC NL SE
APPLICATION INFO.: WO 1992-US5463 A 19920626

PRIORITY INFO.: US 1991-723,009 19910628

L35 ANSWER 6 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1991019733 PCTFULL ED 20020513
TITLE (ENGLISH): DERIVATIVES OF TETRAPEPTIDES AS CCK AGONISTS
TITLE (FRENCH): DERIVES DE TETRAPEPTIDES EN TANT QU'AGONISTES DE CHOLECYSTOKININE
INVENTOR(S): SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kona;
HOLLADAY, Mark, W.;
LIN, Chun, W.;
NELLANS, Hugh, N.
PATENT ASSIGNEE(S): ABBOTT LABORATORIES
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9119733	A1	19911226

DESIGNATED STATES W: AT BE CA CH DE DK ES FR GB GR IT JP LU NL SE
APPLICATION INFO.: WO 1991-US4458 A 19910620
PRIORITY INFO.: US 1990-541,230 19900620
US 1991-713,010 19910614

L35 ANSWER 7 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1990006937 PCTFULL ED 20020513
TITLE (ENGLISH): DERIVATIVES OF TETRAPEPTIDES AS CCK AGONISTS
TITLE (FRENCH): DERIVES DE TETRAPEPTIDES UTILISES COMME AGENTS REPRODUISANT L'ACTIVITE DE LA CCK
INVENTOR(S): SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kong
PATENT ASSIGNEE(S): ABBOTT LABORATORIES;
SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kong
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9006937	A1	19900628

DESIGNATED STATES W: BE CH DE ES FR GB IT JP NL SE US
APPLICATION INFO.: WO 1989-US5673 A 19891218
PRIORITY INFO.: US 1988-287,955 19881221

L35 ANSWER 8 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1990006128 PCTFULL ED 20020513
TITLE (ENGLISH): METHODS AND COMPOSITIONS FOR INHIBITING PLATELET AGGREGATION
TITLE (FRENCH): METHODES ET COMPOSITIONS POUR INHIBER L'AGREGATION DES PLAQUETTES
INVENTOR(S): MARAGANORE, John, M.;
JAKUBOWSKI, Joseph, A.
PATENT ASSIGNEE(S): BIOGEN, INC.;
TRUSTEES OF BOSTON UNIVERSITY
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9006128	A1	19900614
DESIGNATED STATES W:	DK FI HU JP KR NO		
APPLICATION INFO.:	WO 1989-US849	A	19890302
PRIORITY INFO.:	US 1988-280,618		19881205

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=> s l35 and cck
          2003 CCK
            36 CCKS
          2007 CCK
                 (CCK OR CCKS)
L36           5 L35 AND CCK

=> d ibib 1-5
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L36 ANSWER 1 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER: 1996039161 PCTFULL ED 20020514

TITLE (ENGLISH): MULTI-TYROSINATED SOMATOSTATIN ANALOGS

TITLE (FRENCH): ANALOGUES DE LA SOMATOSTATINE CONTENANT PLUSIEURS DE TYROSINES

INVENTOR(S): COY, David, H.;
WOLTERING, Eugene, A.;
O'DORISIO, M., Sue;
O'DORISIO, Thomas, M.;
MURPHY, William, A.

PATENT ASSIGNEE(S): THE ADMINISTRATORS OF THE TULANE EDUCATIONAL FUND ;
THE OHIO STATE UNIVERSITY RESEARCH FOUNDATION;
THE LOUISIANA STATE UNIVERSITY MEDICAL CENTER FOUNDATION;
CHILDREN'S HOSPITAL, INC.

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9639161	A1	19961212
DESIGNATED STATES W:	AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG		
APPLICATION INFO.:	WO 1996-US8437	A	19960603
PRIORITY INFO.:	US 1995-8/462,223		19950605

L36 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER: 1994023724 PCTFULL ED 20020513

TITLE (ENGLISH): MEMBRANE-PERMEANT SECOND MESSENGERS

TITLE (FRENCH): MESSAGERS SECONDAIRES S'INFILTRANT DANS LA MEMBRANE CELLULAIRE

INVENTOR(S): TSIEN, Roger, Y.;
SCHULTZ, Carsten

PATENT ASSIGNEE(S): THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9423724	A1	19941027
DESIGNATED STATES W:	AU BB BG BR BY CA CN CZ FI HU JP KP KR KZ LK LV MG MN		

MW NO NZ PL RO RU SD SI SK UA UZ VN AT BE CH DE DK ES
FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN
ML MR NE SN TD TG

APPLICATION INFO.: WO 1994-US3889 A 19940408
PRIORITY INFO.: US 1993-45,585 19930409

L36 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1993008842 PCTFULL ED 20020513
TITLE (ENGLISH): HEMOGLOBINS AS DRUG DELIVERY AGENTS
TITLE (FRENCH): HEMOGLOBINES UTILISEES COMME AGENTS ADMINISTRATEURS DE MEDICAMENTS

INVENTOR(S): ANDERSON, David, C.;
MATHEWS, Antony, James

PATENT ASSIGNEE(S): SOMATOGEN, INC.;
ANDERSON, David, C.;
MATHEWS, Antony, James

LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9308842	A1	19930513

DESIGNATED STATES
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK
LU MG MN MW NL NO PL RO RU SD SE UA US AT BE CH DE DK
ES FR GB GR IE IT LU MC NL SE BF BJ CF CG CI CM GA GN
ML MR SN TD TG

APPLICATION INFO.: WO 1992-US9713 A 19921106
PRIORITY INFO.: US 1991-789,177 19911108
US 1991-789,179 19911108

L36 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1991019733 PCTFULL ED 20020513
TITLE (ENGLISH): DERIVATIVES OF TETRAPEPTIDES AS CCK AGONISTS
TITLE (FRENCH): DERIVES DE TETRAPEPTIDES EN TANT QU'AGONISTES DE CHOLECYSTOKININE

INVENTOR(S): SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kona;
HOLLADAY, Mark, W.;
LIN, Chun, W.;
NELLANS, Hugh, N.

PATENT ASSIGNEE(S): ABBOTT LABORATORIES
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9119733	A1	19911226

DESIGNATED STATES
W: AT BE CA CH DE DK ES FR GB GR IT JP LU NL SE
APPLICATION INFO.: WO 1991-US4458 A 19910620
PRIORITY INFO.: US 1990-541,230 19900620
US 1991-713,010 19910614

L36 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1990006937 PCTFULL ED 20020513
TITLE (ENGLISH): DERIVATIVES OF TETRAPEPTIDES AS CCK AGONISTS
TITLE (FRENCH): DERIVES DE TETRAPEPTIDES UTILISES COMME AGENTS REPRODUISANT L'ACTIVITE DE LA CCK

INVENTOR(S): SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kong

PATENT ASSIGNEE(S): ABBOTT LABORATORIES;
SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kong
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9006937	A1	19900628

DESIGNATED STATES
W: BE CH DE ES FR GB IT JP NL SE US
APPLICATION INFO.: WO 1989-US5673 A 19891218
PRIORITY INFO.: US 1988-287,955 19881221

=> d ibib kwic 5

L36 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1990006937 PCTFULL ED 20020513
TITLE (ENGLISH): DERIVATIVES OF TETRAPEPTIDES AS CCK AGONISTS
TITLE (FRENCH): DERIVES DE TETRAPEPTIDES UTILISES COMME AGENTS REPRODUISANT L'ACTIVITE DE LA CCK
INVENTOR(S): SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kong
PATENT ASSIGNEE(S): ABBOTT LABORATORIES;
SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kong
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9006937	A1	19900628

DESIGNATED STATES
W: BE CH DE ES FR GB IT JP NL SE US
APPLICATION INFO.: WO 1989-US5673 A 19891218
PRIORITY INFO.: US 1988-287,955 19881221
TIEN DERIVATIVES OF TETRAPEPTIDES AS CCK AGONISTS
TIFR DERIVES DE TETRAPEPTIDES UTILISES COMME AGENTS REPRODUISANT L'ACTIVITE DE LA CCK
ABEN Tetrapeptide analogs are disclosed which possess CCK agonist activity.
ABFR Les analogues de tetrapeptides decrits possedent une activite similaire a la cholecystokinine (CCK).

DETD DERTVATIVES OF-TETRAPEPTIDES AS CCK AGONISTS
This is a continuation-in-part of U.S. Patent Application Serial No. 287,955, filed December 21, 1988.

Technical Field
The present invention relates to novel organic compounds and compositions which mimic the effects of cholecystokinin, caerulein and gastrin, processes for making such compounds, synthetic intermediates employed in these processes and a method for treating gastrointestinal disorders, central nervous. . .

Backaround of thp Tnvention

Cholecystokinin (CCK) is a 39 amino acid polypeptide hormone. CCK and a 33 amino acid fragment of CCK (CCK 33)
were first isolated from hog intestine (Mutt and jorpes, Biochem.]L, 12,Ij 628 (1981)). Recently the CCK 33 fragment has been found in the brain, where it appears to be the precursor of two smaller fragments, an octapeptide CC]K8 and a tetrapeptide CCK 4 (Dockray, Nature 264 402 (1979)).

Existence of these fragments in the cortex of the brain suggests that CCK may be an important neuromodulator of memory, learning and control of the primary sensory and motor functions. CCK and it-s fragments are believed to play an important role in appetite regulation and satiety (Della-Ferat Science 206 471 (1979); Saito et. . . Eating and it-s Disorders, eds.,
Raven Pressr New Yorkf 67 (1984)). Recently,, patients with bulimia were shown to have lower than normal CCK levels in their plasma-(Geracioti, et al., New England Journal of Medici=, 3_12 683 (1988)). An additional role for CCK in the periphery is to regulate the release of insulin., CCK has been shown to increase the levels of insulin when administered to mammals (Rushakoff, et al., J. Clin. Endocrinol, Metab. 65 395. . .

C-terminal fragments of CCK have recently been reported to function as CCK receptor antagonists (Jensen et al Biochem. Biophys. Acta, 757, 250 (1983); Spanarkel, J. Biol. Chem. ZUt 6746 (1983)). Japanese patent application 45/10506 to. . .

In contrast, the present invention relates to tetrapeptide analogs-which function as agonists of CCK activity, CCK agonists are useful in the treatment and prevention of CCK-related disorders of the gastrointestinal, appetite (obesity and bulimia, among others) and insulin regulatory systems of animals, especially man. CCK agonists are also useful as central nervous system suppressants which can exhibit anti-psychotic, neuroleptic, anxiolytic, and anti-convulsant effects, among other effects on. . .

. . .
the Drawinas
Figure I is a plot comparing the mean level of liquid food intake (mls) for rats after chronic administration of vehicle, CCK-8 (10 nmol/kg), or the compound of Example
180 (1 nmol/kg or 10. nm/kg).

Figure 2 is a plot comparing the mean change in body weight (grams) for rats after chronic administration of vehicle, CCK-8 (10 nmol/kg), or the compound of Example
180 (1 nmol/kg or 10 nm/kg),
Summary of the Invention
In accordance with the present invention there are cholecystokinin agonists of the formula.

. . .
IL 1981, p 617)
wherein the Boc or Cbz protected amino acid is treated with a base in the presence of a chelating agent such as a crown ether and then quenched with methyl iodide.

. . .
found: C
61.11r H 6.50F. N 10.89,

The compounds of formula I are CCKagonists which are useful in the treatment and prevention of CCK-related disorders of the gastrointestinal, central nervous, and appetite and insulin regulatory systems of animals and humans. As CCK agonists, they are useful in the treatment and prevention of neuroleptic disorders, tardive dyskinesiat disorders of memory and cognition, Parkinson's disease, Huntington's chorea,. . .

The ability of the compounds of the invention to interact with CCK receptors and to act as CCK agonists can
be demonstrated ja vitro using the following protocols.

CCK8 [Asp-Tyr(SO 3H)-Met-Gly-Trp-
Met-Asp-Phe-NH2], bestatin and phosphoramidon were purchased from Peptide International (Louisville, KY), EGTAr HEPES and BSA were purchased from Sigma Chemical Co.

(St. Louis,, MO), 125 11 - Bolton-Hunter (BH-CCK (specific activity, 2200 Ci/mmol) was obtained from New England Nuclear (Boston, MA). Male guinea pigs, 250 to 32S g, were obtained from Scientific Small Animal Laboratory and Farm (Arlington Heights, IL). Collagenase, code CLSPA was purchased from Worthington (Frehold, New Jersey)
Protocol For Radioligand Binding Experiments in Guinea Pig Cerebral Cortical and
Pancreatic Membrane PreT)arations
Cortical and pancreatic membranes were prepared as described (Lin and Miller; J, Pharmacol,. . .

Incubation Conditions
1 125 I]Bolton-Hu-nter CCK and test compounds were
8
diluted with HEPES-EGTA-salt buffer (see above) containing 0.5% bovine serum albumin (BSA). To 1 mL Skatron polystyrene tubes were added 25 uL of test compounds, 25 uL of [125 IJBH-CCK and 200 uL of membrane suspension. The
8
final BSA concentration was 0.1%. The cortical tissues were incubated at 300C for 150 min.. . . 37'C for 150 min. Incubations were
terminated by filtration using Skatron Cell Harvester and SS32 microfiber filter mats. The specific binding of
125
I IIBH-CCK 8. defined as the difference between binding in
the absence and presence of 1 uM CCK., was 85-90% of total binding in cortex and 90-95% in pancreas. IC 50 s were determined from the Hill analysis. The results. . .

Table 1
125 1aaQ7'Q'L125
Compound of I-BH-CCK 8 I-BH-CCK8
Example Pancreas Cortex
30 270
12 680
10 732
26 238
71 1480
26 1800
32 114
45 35 4700
4 7 50 4 000
4 9 4 1 815

The results indicate that compounds of the invention possess selective affinity for the pancreatic CCK receptors.

Amylase Assay
After the 30 min incubation time, the acini was resuspended in 100 volumes of KRH-BSA buffer, containing 3 uM phosphoramidon and 100 uM bestatin. While stirring, 400 uL of acini were added to 1.5 mL microcentrifuge tubes containing 50 uL of CCK., buffer, or test compounds. The final assay volume was 500 uL. Tubes were vortexed and placed in a 37'C waterbathf under 100%. . .

TABLE 2
Cgmipound of Example Amylase rele=r.----M.4aIIL
5
3
40
80
24
157 ill
180 0.74
The results indicate that compounds of the invention are CCK agonists.

Measurement of PlasMa Insulin in Mice Following Treatment With CCK or a CCK Aaonist
Male mice, 20-30 g. were used in all experiments. The animals were fed with laboratory lab chow and water ad libitum. CCK8 or the CCK agonist compound of this invention was injected into the tail vein. Two minutes later, the animals were sacrificed and the blood was collected. . . 10,000 x g for 2 minutes. The insulin levels were determined in the supernatant, i,e,, plasma, by RIA using kits obtained from Radioassay Systems Laboratory (Carson, CA.) or Novo Biolabs (Danbury, CT.).

Agonists On Insulin Secretion in Nice
% Increase In Insulin
Dose Secretion versus
Com-pound of Examr)le (nmole/kcr)]alinC Control
157 10 41
100 112
180 100 238
CCK8 3 65
10 85
30 90
100 70
The results indicate that compounds of the invention stimulate insulin secretion in yjy.Q.

Table 4
Suppression of Locmotor-Activity in Mice Followincr
IP Administration of CCK Acronists
Comvound of ExamPI& Minimal Effective Dose
CCK 0.001 micromol/kg
106 1.0 micromol/kg
157 0.03 micromol/kg
180 0.01 micromol/kg
Table 5
Sur)r)ression of Locgmotor Activity in Mice Following JCV Administration of CCK Agonists
Comnound of Exam-ole Minimal Effective Dose

CCK8 3.0 nmol/mouse
106 10.0 nmol/mouse
157 30.0 nmol/mouse
180 1.0 nmol/mouse
The results of these tests indicate that compounds of the invention suppress locomotor activity. . .

food intake. Five minutes prior to their one hour free feeding (Purina Rat Chow), the animals were injected (i,p,) with either vehicle, CCK 8 or the compound of Example 106. The amount of food consumed was measured after subtraction of spillage. The results of this test are. . .

AdMinistration of CCK Agonists
Compound Dose Mean Food Intake
vehicle ... 9,40 grams
C-CK 20 ug/kg 6.56 grams
Example 106 1,0 mg/kg 3.49 grams
Example 106 3.0 mg/kg. . .

When a compound of formula I is used as an agonist of CCK or gastrin in a human subject, the total daily dose administered in single or divided doses may be in amounts, for example,. . .

CLMEN 5 A method for mimicking the effects of CCK on CCK receptors comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 1,

7 A CCK agonist composition comprising a pharmaceutical carrier and a therapeutically effective amount of a compound of Claim 1.

```
=> s CCK and (DOTA or DTPA)
          2003 CCK
            36 CCKS
          2007 CCK
                 (CCK OR CCKS)
          1767 DOTA
             5 DOTAS
          1768 DOTA
                 (DOTA OR DOTAS)
          5576 DTPA
            12 DTPAS
          5579 DTPA
                 (DTPA OR DTPAS)
L37         79 CCK AND (DOTA OR DTPA)

=> s l37 not py>1996
        935225 PY>1996
L38          5 L37 NOT PY>1996

=> d ibib kwic 1-5

L38    ANSWER 1 OF 5     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        1996005861 PCTFULL  ED 20020514
TITLE (ENGLISH):         COMPOSITIONS AND METHODS FOR THE TREATMENT OF BODY
                         WEIGHT DISORDERS, INCLUDING OBESITY
TITLE (FRENCH):          COMPOSITIONS ET PROCEDES DE TRAITEMENT DES TROUBLES
                         INHERENTS AU POIDS CORPOREL, DONT L'OBESITE
INVENTOR(S):             TARTAGLIA, Louis, A.
```

PATENT ASSIGNEE(S): MILLENIUM PHARMACEUTICALS, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9605861	A1	19960229

DESIGNATED STATES
W: AU CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1995-US10918 A 19950823
PRIORITY INFO.: US 1994-294,522 19940823
US 1995-470,868 19950606

DETD . . . These include but are not limited to the intracellular domain of receptors for such hormones as neuropeptide Y, galanin, interostatin, insulin, and CCK. Total genomic or cDNA sequences are fused to the DNA encoding an activation domain. This library and a plasmid encoding a hybrid of. . .

. . .
Eu, or others
of the lanthanide series. These metals can be attached to the antibody using such metal chelating groups as diethylenetriaminepentacetic acid (DTPA) or ethylenediaminetetraacetic acid (EDTA).

L38 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995024426 PCTFULL ED 20020514
TITLE (ENGLISH): A NOVEL EXPRESSION-CLONING METHOD FOR IDENTIFYING TARGET PROTEINS FOR EUKARYOTIC TYROSINE KINASES AND NOVEL TARGET PROTEINS
TITLE (FRENCH): NOUVEAU PROCEDE D'EXPRESSION-CLONAGE UTILISE POUR IDENTIFIER DES PROTEINES A CIBLES DES TIROSINE-KINASES EUKARYOTES, ET NOUVELLES PROTEINES CIBLES
INVENTOR(S): SCHLESSINGER, Joseph;
SKOLNIK, Edward, Y.;
MARGOLIS, Benjamin, L.
PATENT ASSIGNEE(S): NEW YORK UNIVERSITY
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9524426	A1	19950914

DESIGNATED STATES
W: AM AU BB BG BR BY CA CN CZ EE FI GE HU JP KE KG KR KZ LK LR LT LV MD MG MN MW MX NO NZ PL RO RU SD SG SI SK TJ TT UA UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.: WO 1995-US3385 A 19950313
PRIORITY INFO.: US 1994-208,887 19940311

DETD . . . lanthanide series. These metals can be attached to the peptide probe or anti-target protein antibody using such metal chelating groups as diethylenetriaminepentaacetic acid (DTPA) or ethylenediaminetetraacetic acid (EDTA).

. . .
know how to varv the aonrorrlate
is parameters without undue ex-oerimentation. Furthermore , general methods in this area are set- forth in Sa:L=cck et al - (sunra)
Materials of which solid phase carrier can be made include, but are not limited to, nitrocellulose,

cellulose, paner, substituted polystyrenes, acrylonitriles,. . .

L38 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995024225 PCTFULL ED 20020514
TITLE (ENGLISH): POLYCHELANTS
TITLE (FRENCH): POLYCHELATEURS
INVENTOR(S): MARGERUM, Lawrence;
CARVALHO, Joan;
GARRITY, Martha;
FELLMANN, Jere, Douglas
PATENT ASSIGNEE(S): NYCOMED SALUTAR, INC.;
COCKBAIN, Julian, Roderick, Michaelson;
MARGERUM, Lawrence;
CARVALHO, Joan;
GARRITY, Martha;
FELLMANN, Jere, Douglas
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9524225	A1	19950914

DESIGNATED STATES
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SG SI SK TJ TT UA UG US UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1995-GB464	A	19950303
PRIORITY INFO.:	GB 1994-9404208.2		19940304

DETD Thus, Krejcarek et al (supra) disclosed how polyaminopolycarboxylic acid (PAPCA) chelants, specifically DTPA (diethylenetriaminepentaacetic acid) could be conjugated to a protein, such as human serum albumin (HSA), by reaction of the triethylamine salt of the PAPCA. . .

Unger et al. in Investigative Radiology 20:693 (1985) analyzed tumor enhancement for magnetic resonance imaging using an anti-CEA monoclonal antibody conjugated with Gd-DTPA. They found no tumor enhancement when 4 Gd atoms were bound per antibody molecule, and predicted that a far greater ratio of. . .

Thus Hnatowich et al, (supra) used the cyclic anhydride of the chelant DTPA to attach it to a protein. . .

. . .
has thus been used
to produce bifunctional polychelants in which the chelant moieties are residues of open chain PAPCAs, such as EDTA and DTPA, and in which the backbone molecule is a polyamine such as polylysine or polyethyleneimine.

Thus for example Manabe et al. in Biochemica et Biophysica Acta 883: 460-467 (1986) reported attaching up to 105 DTPA residues onto a poly-L-lysine backbone using the cyclic anhydride method and also attaching polylysine-polyDTPA polychelants onto monoclonal antibody (anti-HLA IgGj) using a 2-pyridyl disulphide linker achieving a substitution of up to about 42.5 chelants (DTPA resi]_-:-.-]s) per site-specific macromolecule. Torcrilin et al. in Hybridoma 6:229-240 (1987) also reported attaching DTPA and EDTA to

polyethyleneimine and polylysine backbones which were then attached to a myosin-specific monoclonal antibody, or its Fab fragment, to produce bifunctional polychelants. . .

. . .

chelant moieties in the polychelants of the invention may be residues of any of the conventional macrocyclic chelants such as for example DOTA, TETA, D03A. etc, The macrocyclic skeleton, as mentioned above, preferably has 9 to 25 ring members and conveniently is an optionally oxygen or. . . pendent groups which participate in metal chelation, for example C1-6alkyl groups carrying hydroxyl, amino, phosphonate, or phosphinate or more preferably carboxyl groups. D03A and DOTA derived macrocycles are especially preferred, i,e. groups of formula
HOOC--\F-] X]--COOH HOOC--\F7 /-COOH
N N-] and [-N
EN N N N
\-COOH HOOC--/. . .

Exemplary polyazacycloalkanepolycarboxylates include 1 7,10-tetraazacyclododecanetetraacetic acid (DOTA), 1,4,7,10-tetraazacyclododecane 4,7-triacetic acid (D03A), 1-oxa-4,7,10-triazacyclododecanetriacetic acid (DOXA), 1,4,7-triazacyclononanetriacetic acid (NOTA) and 1 8,11-tetraazacyclotetradecanetetraacetic acid (TETA), Additionally, the novel tetraazacycloalkanepolycarboxylates, DOTA-N(2-aminoethyl)amide and DOTA-N(4-aminophenethyl)amide are also contemplated,
The preparation of the tetraazacycloalkanepoly-carboxylate ligands is well known. Synthesis of DOTA is described in U.S. Patent No. 4,647,447 (Gries et al,), U.S. Patent No, 4,639,365 (Sherry) and by Desreux et al.

in Inorg. Chem. 19:1319 (1980). Additionally, DOTA is available commercially from Parish Chemical Co,, Orem, UT, USA. Preparation of D03A is described in EP-A-292689 (Squibb). Desreux, Inorg. Chem., 19:1319. . . al, Inorg. Chem, 26:3458 (1987)
and Meares et al, Acc. Chem. Res., 17:202 (1984) describe the properties and chemistry of tne macrocyclic ligands DOTA, NOTA, TETA and their backbone-derivatized analogues, including the preparation of NOTA and TETA.

U.S. Patent No, 4,678,667 (Meares et al.) teaches the preparation of a number of macrocyclic, side chain-derivatized ligands including DOTA and TETA.

Derivatization of DOTA to form DOTA
-N(2-aminoethyl)amide
and DOTA-N(4-aminophenethyl)amide is described in detail hereinafter in Examples 2 and 3, respectively, The above cited references and all other references mentioned herein are hereby. . .

. . .

be taken with the lanthanide ions to maintain the pH below 8 to avoid precipitation of the metal hydroxide. Metal incorporation into DOTA derived and related macrocylic chelant moieties will normally be a slow process, as described in the references cited below. Specific examples of the. . .

Med., 3:808 (1986) and WO-A-87/06229 describe

incorporation of Gd(III) into DOTA. A method of preparing Bi and Pb complexes of DOTA is described by Kumar et al, J. Chem. Soc. Chem. Commun., 3:145 (1989).

. . .

reduction of 99Tc with Sn in the presence of a weakly coordinating ligand such as glucoheptonate prior to complexation with chelants such as DOTA. These methods are well known in the radiopharmaceutical art 67CU utilizes tetraamine chelates such as tet A or tet B (see Bhardaredj. . .

CCK and hexapeptides), proteins (such as lectins, asialofetuin, polyclonal IgG, blood clotting proteins (e.g. hirudin), lipoproteins and glycoproteins), hormones, growth factors, and clotting factors. . .

. . .

In general, known methods can be used to join the macrocyclic chelants to backbone molecules. While for preferred macrocyclic chelants, such as DOTA, the conventional mixed anhydride and cyclic anhydride conjugation techniques are ineffective, it has been found that.modifying the mixed anhydride procedure by reacting a polycarboxylic. . .

For macrocycles with a pendant carboxylate, including but not limited to DOTA, TETA, TRITA (1,4,7,10-tetraazacyclotridecanetetraacetic acid) and NOTA, one of the carboxylates can form an entity which can react with a primary amine group. . .

. . .

linked to a backbone molecule through a non-coordinating primary amine group. Macrocyclic chelants having a non-coordinating primary amine group include primary amine side-chain-derivatized DOTA macrocycles, primary amine-derivatized D03A, and primary amine-derivatized hexaaza and octaaza macrocycles and macrobicycles (the HAMs.

. . .

for example, physiologically biocompatible buffers (as for example, tromethamine hydrochloride), additions (e,g,, 0.01 to 10 mole percent) of chelants (such as, for example, DTPA, DTPA-bisamide or non-complexed magnifier polychelant) or calcium chelate complexes (as for example calcium DTPA, CaNaDTPA-bisamide, calcium-magnifier polychelant or CaNa salts of magnifier polychelants), or, optionally, additions (e.g., 1 to 50 mole percent). of calcium or sodium salts (for. . .

L38 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER: 1995005842 PCTFULL ED 20020514

TITLE (ENGLISH): METHOD AND DEVICE FOR TREATING GASTROINTESTINAL MUSCLE DISORDERS AND OTHER SMOOTH MUSCLE DYSFUNCTION

TITLE (FRENCH): PROCEDE ET DISPOSITIF POUR TRAITER LES TROUBLES MUSCULAIRES GASTRO-INTESTINAUX ET AUTRES DYSFONCTIONNEMENTS DES MUSCLES LISSES

INVENTOR(S): PASRICHA, Pankaj, J.;
KALLOO, Anthony, N.

PATENT ASSIGNEE(S): THE JOHNS HOPKINS UNIVERSITY

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9505842	A1	19950302

DESIGNATED STATES
W: CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1994-US9759 A 19940823
PRIORITY INFO.: US 1993-112,088 19930826

DETD Figs. 3A and B show the effect of intrasphincteric injection of BoTx on LES response to cholecystokinin octapeptide (CCK)

. . .
response of the LES to the IV administration of edrophonium (Tensilcn; ICN Pharmaceuticals Inc., Costa Mesa, CA) and cholecystokinin octapeptide (CCK-8) (Kinevac; ER Squibb amp;Sons, Princeton, NJ) in three
additional piglets was also measured. LES pressures, measured by a DENTSLEEVE, were recorded in response to IV edrophonium (5 mg). After a SUBSTITUTE SHEET (RULE 26)
washout period of 10 minutes, CCK (5 µg IV) was then administered.
Subsequently, BoTx was injected into the LES, as described above, and the
experiment was. . .

Intrasphincteric BoTx also altered the response of the LES to CCK
(Figure 3). In untreated piglets, CCK did not cause any significant change in
LES pressure. However, after intrasphincteric BoTx injection, a significant
increase in LES pressure was seen in response to CCK. It should be noted that
despite what was felt to be an adequate washout period (10 minutes) in between
injections, basal. . .

. . .
retention studies
After an overnight fast, patients were asked to ingest a corn-flake meal with milk containing 0.531 mci 99 aiTc DTPA. Subsequently, serial dynamic
images were obtained with the subject sitting erect in front of a gamma camera.
Retention was expressed. . .

L38 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1993006868 PCTFULL ED 20020513
TITLE (ENGLISH): DENDRIMERIC POLYCHELANTS
TITLE (FRENCH): POLYCHELATEURS DENDRIMERES
INVENTOR(S): WATSON, Alan, D.
PATENT ASSIGNEE(S): COCKBAIN, Jilian, Roderick, Michaelson;
NYCOMED SALUTAR, INC.;
WATSON, Alan, D.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9306868	A1	19930415

DESIGNATED STATES
W: AU BB BG BR CA CS FI HU JP KP KR LK MG MN MW NO PL RO RU SD US AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE BF BJ CF CG CI CM GA GN ML MR SN TD TG
APPLICATION INFO.: WO 1992-EP2308 A 19921006
PRIORITY INFO.: US 1991-7/772,349 19911007
ABEN . . . chelates which are useful in diagnostic imaging and in radiotherapy and which comprise a plurality of macrocyclic chelant moieties, e.g. DOTA
residues, conjugated to an up to fifth generation dendrimer backbone

molecule, e.g. a starburst
dendrimer. To produce a site-specific polychelate,. . .

ABFR . . . utilises dans l'imagerie diagnostique et en radiotherapie. Ils comportent une pluralite de fractions de chelateurs macrocycliques, par exemple
des restes DOTA, conjugues a une molecule de squelette dendrimere dont la generation va jusqu'a la cinquieme, par exemple un dendrimere en etoile.. . .

DETD . . . paramagnetic metal ion
chelates of bifunctional chelants for use as MRI contrast agents,
Thus, Krejcarek et al (supra) disclosed how polyaminopolycarboxylic acid (PAPCA) chelants, specifically DTPA (diethylepetriaminepentaacetic acid) could be conjugated to a protein, such as human serum albumin (HSA), by reaction of the triethylamine salt of the PAPCA. . .

. . .
152:571 (1988))e
Unger et al, in Investigative Radiology 20:693-(1985) analyzed tumor enhancement for magnetic resonance imaging using an anti-CEA monoclonal antibody conjugated with Gd-DTPA* They found no tumor enhancement when 4 Gd atoms were bound per antibody molecule, and predicted that a far greater ratio of. . .

Thus Hnatowich et al, (supra) used the cyclic anhydride of the chelant DTPA to attach it to a protein, This, is a relatively simple one-step synthesis procedure which as a result has been used by. . .

. . .
has
thus been used to produce bifunctional polychelants in which the chelant moieties are residues of open chain PAPCAs,, such as EDTA and DTPA,, and in which the backbone molecule is a polyamine such as polylysine or polyethyleneimine. Thus for example Manabe et al, in Biochemica. et Biophysica Acta 883: 460-467 (1986) reported attaching up to 105 DTPA residues onto a poly-L-lysine backbone using the cyclic anhydride method and also attaching polylysine-polyDTPA polychelants onto monoclonal antibody (anti-HLA IgGj) using a 2-pyridyl disulphide linker achieving a substitution of up to about 42,5 chelants (DTPA residues) per site-specific macromolecule. Torchlin et al. in Hybridoma 6:229-240 (1987) also reported attaching DTPA and EDTA to polyethyleneimine and polylysine backbones which were then attached to a myosin-specific monoclonal antibody, or its Fab fragment, to produce bifunctional polychelants. . .

. . .
diagnosis and therapy, due in part
to their unique localization in the body, The monomeric chelates presently used for MRI contrast enhancement (e.g,, Gd(DTPA)2-,, Gd(DOTA)'-) have in vivo applications
related to their specific, rapid biodistribution, localizing these chelates in the extravascularl extracellular spaces of the body. The size. . .

Exemplary polyazacycloalkanepolycarboxylates include 1,4,7,10-tetraazacyclododecanetetraacetic acid (DOTA), 1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid (DO3A), I-oxa-4,7,10-triazacyclododecanetriacetic

acid (DOXA), 1.4,7-triazacyclononanetriacetic acid (NOTA) and 1.4,8,11-tetraazacyclotetradecanetetraacetic acid (TETA), Additionally, the novel - tetraazacycloalkanepolycarboxylates, DOTA-N(2-aminoethyl)amide and DOTA-N(4-aminophenethyl)amide are also contemplated.

The preparation of,the tetraazacycloalkanepoly-carboxylate ligands is well known. Synthesis of DOTA is described in U,S. Patent No, 4,647,447 (Gries et al,), U.S, Patent No, 4,639,365 (Sherry) and by Desreux et al, in Inorg. Chem, .19:1319 (1980). Additionally, DOTA is available commercially from Parrish Chemical Co,, Orem, UT, USA. Preparation of D03A is described in EP-A-292689 (Squibb). Desreux, Inorg. Chem,, 19:1319. . . et al, Inorg, Chem, 26:3458 (1987)
and Meares et al, Acc, Chem, Res,, 17:202 (1984) describe theproperties and chemistry of the macrocyclic ligands DOTA, NOTA, TETA and their backbone-derivatized analogues, including the preparation of NOTA and TETA, U.S. Patent No. 4,678,667 (Meares et al,) teaches the preparation of a number of macrocyclic, side chain-derivatized ligands including DOTA and TETA, Derivatization of DOTA to form DOTA -N(2-aminoethyl)amide
and DOTA-N(4-aminophenethyl)amide is described in detail hereinafter in Examples 2 and 3, respectively. The above cited references and all other references mentioned herein are hereby. . .

. . .
acids, oligopeptides (e.g. hexapeptides), molecular recognition units (MRU's), single chain antibodies (SCA's), proteins, Fab fragments, and antibodies. Examples of site-directed molecules include polysaccharides (e,g, CCK and hexapeptides), proteins (such as lectins, asialofetuin, polyclonal IgG, blood clotting proteins (e.g. hirudin), lipoproteins and glycoproteins), hormones, growth factors, and clotting factors (such. . .

. . .
molecule
in general, known methods can be used to join the macrocyclic chelants to backbone molecules. While for preferred macrocyclic chelants, such as DOTA, the conventional mixed anhydride and cyclic anhydride conjugation techniques are ineffective, it has been found that modifying the mixed anhydride procedure by reacting a. . .

For macrocycles with a pendant carboxylate, including but not limited to DOTA, TETA, TRITA (1.4,7,10-tetraazacyclotridecanetetraacetic acid) and NOTA, one of the carboxylates can form an entity which can react with a primary amine group of. . .

. . .
linked to the
backbone polymer through a non-coordinating primary amine group. Macrocyclic chelants having a non-coordinating primary amine group include primary amine side-chain-derivatized DOTA macrocycles, primary amine-derivatized D03A. and primary amine-derivatized hexaaza and octaaza. macrocycles and macrobicycles (the HAMsr sepulchrates and sarcophagines) as well as the. . .

Metal incorporation into DOTA derived and related

macrocylic chelant moieties will normally be a slow process, as described in the references cited below, Specific examples of the. . .

Ned,, 3:808 (1986) and WO-A-87/06229 describe incorporation of Gd(III) into DOTA, A method of preparing Bi and Pb complexes of DOTA is described by Kumar et alf J. Chem, Soc, Chem, Commun., 3:145 (1989)o The above references are incorporated herein by reference in their. . .

. . .

reduction of 99mTc
with Sn in the presence of a weakly coordinating ligand such as glucoheptonate prior to complexation with chelants such as DOTA, These methods are well known in the radiopharmaceutical art. OCu utilizes tetraamine chela]tes such as tet A or tet B (see Bhardaredj. . .

. . .

for example, physiologically
biocompatible buffers (as for example, tromethamine hydrochloride), additions (e.g., 0,01 to 10 mole percent) of chelants (such as, for example, DTPA, DTPA
-
bisamide or non-complexed magnifier polychelant) or calcium chelate complexes (as for example calcium DTPA, CaNaDTPA-bisamide, calcium-magn-ifier polychelant or CaNa salts of magnifier polychelants),, or, optionally, additions (e.g., I to 50 mole percent) of calcium or sodium salts (for. . .

EXAMPLE I
Preparation of DOTA Carboxycarbonic Anhydride
DOTA(0*808 g-I 2,0 mmol) was suspended in 5.0 ml of anhydrous acetonitrile, Tetramethylguanidine (1eOO mli, 8.0 mmol) was added and the mixture stirred under an atmosphere of nitrogen for about 5 minutes at ambient temperature until the DOTA was dissolved, The resulting solution was cooled to -250C under an atmosphere of nitrogen and stirred while adding 0,260 ml (2,0 mmol). . .

The resulting slurry was stirred for I hour at -25 C4
EXAMPLE 2
Preparation of DOTA-N(2-aminoethVl)amide
To the cold slurry from Example 1 was added a solution of mono-BOC-ethylenediamine (0,320g, 2mmol) in 2 ml acetonitrile and the mixture stirred. . . afforded 0.35g of a semi-
crystalline glass. IH NMR demonstrated the expected
product, as well as some residual acetate (from chromatography),
EXAMPLE 3
Preparation of DOTA-N(4-aminoDhenethvl)amide
To the cold slurry from Example 1 is added a solution of 4-nitrophenethylamine (0,332g, 2mmol) in 4.0 ml acetonitrile, The mixture is stirred. . . and pH adjusted to 1015 with NaOH to form a mixture which is extracted with ethyl acetate to remove unreacted amine, The product,
DOTA-N-(41-nitrophenethyl)amide, is isolated by ion exchange chromatography on DOWEX AGI-XS resin.

. . .

ceases to drop, The
product is isolated by filtering off catalyst and evaporating the filtrate to dryness,
EXAMPLE 4
Activation of Amino Group of DOTA-N(2-aminoethyl)amide

with Thiophosgene - Conversion to Isothiocyanate Groups
An aqueous solution of the product prepared in
Example 2 is added to an equal volume. . .

. . .
The procedure is repeated, substituting the product
of Example 3 for the product of Example 2,
EXAMPLE 5
Activation of Amino Group of DOTA-N(2-Aminoethyl)Amide
with Bromoacetyl Chloride - Conversion to Bromoacetamide
Grou'ps
An aqueous solution of the product prepared in
Example 2 (20mg/ml) which also contains triethylamine
(20mg/ml) is. . .

EXAMPLE 13
Preparation of - PAMAM - Poly DOTA
The G2.0 PAMAM dendrimer prepared in Example 10 (log,
0.01 mol) is combined with 12 equivalents of DOTA
carboxycarbonic anhydride (0,13 mol) prepared as in
Example 1, by slowly mixing a precooled (00 C)
acetonitrile solution (20 ml) of dendrimer to the DOTA
mixed anhydride slurry over 10 minutes and gradually
allowing the reaction mixture to warm to ambient
temperature. The reaction mixture is worked up. . .

EXAMPLE 17
Preparation of DOTA-G3 Dendrimer magnifier
An acetonitrile solution of tris-t-butyl-DO3A and
ClCH2CONHCH2(C6H4)pNO2 (Example 16) are heated at 65DC for
24 hours, The chelant-linker product is isolated. . .

CLMEN. . . compound according to any one of claims 1 to 13
wherein said macrocyclic chelants are selected from the
residues of 1,4,7,10- tetraazacyclododecanetetraacetic
acid (DOTA),
1 7,10-tetraazacyclododecane 4 triacetic acid
(DO3A), I-oxa 7,10-triazacyclododecane-triacetic
acid (DOXA), 1 7-triazacyclononanetriacetic acid
(NOTA), 11408fll-tetraazacyclotetradecanetetraacetic
acid (TETA), DOTA-N(2-aminoethyl)amide and DOTA-N(4-
aminophenethyl)amide.

=>

---Logging off of STN---

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=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	74.85	210.85
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-3.00

STN INTERNATIONAL LOGOFF AT 14:05:21 ON 07 DEC 2006

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
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NEWS 3	AUG 09	INSPEC enhanced with 1898-1968 archive
NEWS 4	AUG 28	ADISCTI Reloaded and Enhanced
NEWS 5	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 6	SEP 11	CA/CAplus enhanced with more pre-1907 records
NEWS 7	SEP 21	CA/CAplus fields enhanced with simultaneous left and right truncation
NEWS 8	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 9	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 10	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 11	SEP 28	CEABA-VTB classification code fields reloaded with new classification scheme
NEWS 12	OCT 19	LOGOFF HOLD duration extended to 120 minutes
NEWS 13	OCT 19	E-mail format enhanced
NEWS 14	OCT 23	Option to turn off MARPAT highlighting enhancements available
NEWS 15	OCT 23	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 16	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 17	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 18	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 19	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 20	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 21	NOV 13	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 22	NOV 20	CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS 23	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 24	NOV 20	CA/CAplus patent kind codes will be updated
NEWS 25	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 26	DEC 11	CAS REGISTRY chemical nomenclature enhanced

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

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     as well as in synaptic membranes.
IT   6667-50-1   17650-98-5   20988-63-0 25126-32-3
     25679-24-7   35144-91-3   78137-39-0   78151-11-8
     RL: PRP (Properties)
        (degradation of, by brain synaptosomes)


=> d his

     (FILE 'HOME' ENTERED AT 13:35:48 ON 07 DEC 2006)

     FILE 'REGISTRY' ENTERED AT 13:36:14 ON 07 DEC 2006
L1           136 S DY'NLE'GW'NLE'DF/SQSP
L2           424 S DYMGWMDF/SQSP

     FILE 'CAPLUS' ENTERED AT 13:39:00 ON 07 DEC 2006
L3            84 S L1
L4             0 S DPTA AND L3
L5             5 S DOTA AND L3
L6        134722 S CHELAT?
L7            12 S L6 AND L3
L8             0 S L7 NOT PY>1997
L9             1 S L7 NOT PY>1998
L10         4485 S L2
L11           49 S L10 AND L6
L12           20 S L11 NOT PY>1997
L13           20 S L11 NOT PY>1996
L14        14458 S METAL CHELAT?
L15            3 S L14 AND L10

=> s l10 and (DPTA or DOTA)
           347 DPTA
             1 DPTAS
           347 DPTA
                (DPTA OR DPTAS)
          1203 DOTA
L16           4 L10 AND (DPTA OR DOTA)

=> d ibib 1-4

L16  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2004:702005  CAPLUS
DOCUMENT NUMBER:          141:230668
TITLE:                    Contrast enhanced x-ray phase imaging
INVENTOR(S):              Mattiuzzi, Marco; Arfelli, Fulvia; Menk, Ralf-Hendrik;
                          Rigon, Luigi; Besch, Hans-Juergen
PATENT ASSIGNEE(S):       Bracco Imaging S.P.A., Italy
SOURCE:                   PCT Int. Appl., 38 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2004071535         A1    20040826    WO 2004-EP1213          20040210
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
             BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
             MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG
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EP 1592456 A1 20051109 EP 2004-709594 20040210
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2006517558 T2 20060727 JP 2006-501789 20040210
PRIORITY APPLN. INFO.: US 2003-446986P P 20030213
WO 2004-EP1213 W 20040210

L16 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:43075 CAPLUS
DOCUMENT NUMBER: 135:118839
TITLE: Use of the rat pancreatic CA20948 cell line for the comparison of radiolabelled peptides for receptor-targeted scintigraphy and radionuclide therapy
AUTHOR(S): Bernard, B. F.; Krenning, E.; Breeman, W. A. P.; Visser, T. J.; Bakker, W. H.; Srinivasan, A.; De Jong, M.
CORPORATE SOURCE: Departments of Nuclear Medicine, University Hospital Dijkzigt, Rotterdam, 3015 GD, Neth.
SOURCE: Nuclear Medicine Communications (2000), 21(11), 1079-1085
CODEN: NMCODC; ISSN: 0143-3636
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:271563 CAPLUS
DOCUMENT NUMBER: 129:119669
TITLE: Unsulfated DTPA- and DOTA-CCK analogs as specific high-affinity ligands for CCK-B receptor-expressing human and rat tissues in vitro and in vivo
AUTHOR(S): Reubi, J. C.; Waser, B.; Schaer, J. C.; Laederach, U.; Erion, J.; Srinivasan, A.; Schmidt, M. A.; Bugaj, J. E.
CORPORATE SOURCE: Institute of Pathology, Division of Cell Biology and Experimental Cancer Research, University of Berne, Switz.
SOURCE: European Journal of Nuclear Medicine (1998), 25(5), 481-490
CODEN: EJNMD9; ISSN: 0340-6997
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:594650 CAPLUS
DOCUMENT NUMBER: 127:259530
TITLE: Use of labeled CCK-B receptor ligands for the detection, localization, and treatment of malignant human tumors
INVENTOR(S): Reubi, Jean-Claude
PATENT ASSIGNEE(S): Mallinckrodt Medical, Inc., USA; Reubi, Jean-Claude
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9731657	A2	19970904	WO 1997-US3056		19970225
WO 9731657	A3	19971023			
W: CA, JP, US					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
CA 2247430	AA	19970904	CA 1997-2247430		19970225
EP 885017	A2	19981223	EP 1997-908751		19970225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2000506141	T2	20000523	JP 1997-531108		19970225
US 2004185510	A1	20040923	US 2003-626229		20030724
PRIORITY APPLN. INFO.:			EP 1996-200498	A	19960227
			WO 1997-US3056	W	19970225
			US 1999-125823	B1	19990119
OTHER SOURCE(S):	MARPAT 127:259530				

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L17          9 L10 AND DTPA

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L17 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2004:424231 CAPLUS
DOCUMENT NUMBER:	141:271813
TITLE:	Synthesis and characterization of a sulfated and a non-sulfated cyclic CCK8 analogue functionalized with a chelating group for metal labelling
AUTHOR(S):	De Luca, Stefania; Morelli, Giancarlo
CORPORATE SOURCE:	Centro Interuniversitario per la Ricerca sui Peptidi Bioattivi (CIRPeB) and Dipartimento di Chimica Biologica, Universita di Napoli "Federico II", Naples, 80134, Italy
SOURCE:	Journal of Peptide Science (2004), 10(5), 265-273 CODEN: JPSIEI; ISSN: 1075-2617
PUBLISHER:	John Wiley & Sons Ltd.
DOCUMENT TYPE:	Journal
LANGUAGE:	English
REFERENCE COUNT:	13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2004:254192 CAPLUS
DOCUMENT NUMBER:	142:62411
TITLE:	In Vitro and In Vivo Characterization of Indium-111 and Technetium-99m Labeled CCK-8 Derivatives for CCK-B Receptor Imaging
AUTHOR(S):	Aloj, L.; Panico, M.; Caraco, C.; Del Vecchio, S.; Arra, C.; Affuso, A.; Accardo, A.; Mansi, R.; Tesauro, D.; De Luca, S.; Pedone, C.; Visentin, R.; Mazzi, U.; Morelli, G.; Salvatore, M.
CORPORATE SOURCE:	Istituto di Biostrutture e Bioimmagini, CNR, Naples, Italy
SOURCE:	Cancer Biotherapy & Radiopharmaceuticals (2004), 19(1), 93-98 CODEN: CBRAFJ; ISSN: 1084-9785
PUBLISHER:	Mary Ann Liebert, Inc.
DOCUMENT TYPE:	Journal
LANGUAGE:	English
REFERENCE COUNT:	16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:133309 CAPLUS
DOCUMENT NUMBER: 138:197782
TITLE: Peptides conjugates, their derivatives with metal complexes and use thereof for magnetic resonance imaging (MRI)
INVENTOR(S): Aime, Silvio; Gianolio, Eliana; Morelli, Giancarlo; Pedone, Carlo; Tesauro, Diego; Lattuada, Luciano; Visigalli, Massimo; Anelli, Pier Lucio
PATENT ASSIGNEE(S): Bracco Imaging S.P.A., Italy
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003014157	A2	20030220	WO 2002-EP8382		20020726
WO 2003014157	A3	20031113			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002328981	A1	20030224	AU 2002-328981		20020726
EP 1412383	A2	20040428	EP 2002-764797		20020726
EP 1412383	B1	20061115			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2005510461	T2	20050421	JP 2003-519106		20020726
US 2005008573	A1	20050113	US 2004-485847		20040902
PRIORITY APPLN. INFO.:			IT 2001-MI1708	A	20010803
			WO 2002-EP8382	W	20020726

OTHER SOURCE(S): MARPAT 138:197782

L17 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:609701 CAPLUS
DOCUMENT NUMBER: 136:321340
TITLE: New radiolabeled CCK-8 analogues [Tc-99m-GH-CCK-8 and Tc-99m-DTPA-CCK-8]: preparation and biodistribution studies in rats and rabbits
AUTHOR(S): Ertay, T.; Unak, P.; Bekis, R.; Yurt, F.; Biber, F. Z.; Durak, H.
CORPORATE SOURCE: Dept. of Nuclear Medicine, Dokuz Eylul University, Medical School, Inciralti, Izmir, Turk.
SOURCE: Nuclear Medicine and Biology (2001), 28(6), 667-678
CODEN: NMBIEO; ISSN: 0969-8051
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:402924 CAPLUS
DOCUMENT NUMBER: 131:225550

TITLE: Radiolabeled peptides for targeting cholecystokinin-B/gastrin receptor-expressing tumors
AUTHOR(S): Behr, Thomas M.; Jenner, Niels; Behe, Martin; Angerstein, Christa; Gratz, Stefan; Raue, Friedhelm; Becker, Wolfgang
CORPORATE SOURCE: Department of Nuclear Medicine, Georg-August-University, Gottingen, D-37075, Germany
SOURCE: Journal of Nuclear Medicine (1999), 40(6), 1029-1044
CODEN: JNMEAQ; ISSN: 0161-5505
PUBLISHER: Society of Nuclear Medicine, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:396519 CAPLUS
DOCUMENT NUMBER: 131:200015
TITLE: Tri-t-butyl-DTPA: a versatile synthon for the preparation of DTPA-containing peptides by solid phase
AUTHOR(S): Srinivasan, Ananth; Schmidt, Michelle A.
CORPORATE SOURCE: Mallinckrodt Inc., Hazelwood, MO, 63042, USA
SOURCE: Peptides: Frontiers of Peptide Science, Proceedings of the American Peptide Symposium, 15th, Nashville, June 14-19, 1997 (1999), Meeting Date 1997, 267-268.
Editor(s): Tam, James P.; Kaumaya, Pravin T. P.
Kluwer: Dordrecht, Neth.
CODEN: 67UCAR
DOCUMENT TYPE: Conference
LANGUAGE: English
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:271563 CAPLUS
DOCUMENT NUMBER: 129:119669
TITLE: Unsulfated DTPA- and DOTA-CCK analogs as specific high-affinity ligands for CCK-B receptor-expressing human and rat tissues in vitro and in vivo
AUTHOR(S): Reubi, J. C.; Waser, B.; Schaer, J. C.; Laederach, U.; Erion, J.; Srinivasan, A.; Schmidt, M. A.; Bugaj, J. E.
CORPORATE SOURCE: Institute of Pathology, Division of Cell Biology and Experimental Cancer Research, University of Berne, Switz.
SOURCE: European Journal of Nuclear Medicine (1998), 25(5), 481-490
CODEN: EJNMD9; ISSN: 0340-6997
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:594650 CAPLUS
DOCUMENT NUMBER: 127:259530
TITLE: Use of labeled CCK-B receptor ligands for the detection, localization, and treatment of malignant human tumors
INVENTOR(S): Reubi, Jean-Claude
PATENT ASSIGNEE(S): Mallinckrodt Medical, Inc., USA; Reubi, Jean-Claude
SOURCE: PCT Int. Appl., 61 pp.

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FILE 'HOME' ENTERED AT 13:35:48 ON 07 DEC 2006

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COST IN U.S. DOLLARS SINCE FILE ENTRY 0.21 TOTAL SESSION 0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 13:36:14 ON 07 DEC 2006
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DICTIONARY FILE UPDATES: 6 DEC 2006 HIGHEST RN 914980-83-9

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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L2 424 DYMGWMDF/SQSP

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FILE 'CAPLUS' IS NOT VALID IN THE CURRENT FILE ENVIRONMENT
REGISTRY
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=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL

	ENTRY	SESSION
FULL ESTIMATED COST	59.10	59.31

FILE 'CAPLUS' ENTERED AT 13:39:00 ON 07 DEC 2006
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FILE COVERS 1907 - 7 Dec 2006 VOL 145 ISS 24
FILE LAST UPDATED: 6 Dec 2006 (20061206/ED)

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They are available for your review at:

http://www.cas.org/infopolicy.html

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           1203 DOTA
L5            5 DOTA AND L3

=> d ibib 1-5

L5   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2002:240598  CAPLUS
DOCUMENT NUMBER:          136:272268
TITLE:                    Prochelators for the preparation of radiometal labeled
                          molecules having improved biological properties
INVENTOR(S):              Maecke, Helmut R.; Eisenwiener, Klaus; Powell, Pia
PATENT ASSIGNEE(S):       Mallinckrodt, Inc., USA
SOURCE:                   PCT Int. Appl., 21 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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     WO 2002024235         A2    20020328    WO 2001-EP5483           20010511
     WO 2002024235         A3    20020829
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
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RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2001077488	A5	20020402	AU 2001-77488		20010511
EP 1289571	A2	20030312	EP 2001-955279		20010511
EP 1289571	B1	20040721			
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JP 2004509152	T2	20040325	JP 2002-528305		20010511
AT 271396	E	20040815	AT 2001-955279		20010511
ES 2221903	T3	20050116	ES 2001-1955279		20010511
US 2006233704	A1	20061019	US 2006-533906		20060330
PRIORITY APPLN. INFO.:			EP 2000-110084	A	20000512
			WO 2001-EP5483	W	20010511

OTHER SOURCE(S): MARPAT 136:272268

L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:619258 CAPLUS
DOCUMENT NUMBER: 133:350200
TITLE: A convenient synthesis of novel bifunctional prochelators for coupling to bioactive peptides for radiometal labelling
AUTHOR(S): Eisenwiener, K.-P.; Powell, P.; Macke, H. R.
CORPORATE SOURCE: Department of Radiology, Institute of Nuclear Medicine, Division of Radiological Chemistry, University Hospital, Basel, CH-4031, Switz.
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(18), 2133-2135
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:350200
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:44679 CAPLUS
DOCUMENT NUMBER: 132:319291
TITLE: Preclinical and initial clinical evaluation of 111In-labeled nonsulfated CCK8 analog: A peptide for CCK-B receptor-targeted scintigraphy and radionuclide therapy
AUTHOR(S): De Jong, Marion; Bakker, Willem H.; Bernard, Bert F.; Valkema, Roelf; Kwekkeboom, Dik J.; Reubi, Jean-Claude; Srinivasan, Ananth; Schmidt, Michelle; Krenning, Eric P.
CORPORATE SOURCE: Department of Nuclear Medicine, University Hospital Dijkzigt, Rotterdam, 3015 GD, Neth.
SOURCE: Journal of Nuclear Medicine (1999), 40(12), 2081-2087
CODEN: JNMEAQ; ISSN: 0161-5505
PUBLISHER: Society of Nuclear Medicine, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:271563 CAPLUS
DOCUMENT NUMBER: 129:119669
TITLE: Unsulfated DTPA- and DOTA-CCK analogs as specific high-affinity ligands for CCK-B receptor-expressing human and rat tissues in vitro and

in vivo

AUTHOR(S): Reubi, J. C.; Waser, B.; Schaer, J. C.; Laederach, U.; Erion, J.; Srinivasan, A.; Schmidt, M. A.; Bugaj, J. E.

CORPORATE SOURCE: Institute of Pathology, Division of Cell Biology and Experimental Cancer Research, University of Berne, Switz.

SOURCE: European Journal of Nuclear Medicine (1998), 25(5), 481-490
CODEN: EJNMD9; ISSN: 0340-6997

PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:594650 CAPLUS
DOCUMENT NUMBER: 127:259530
TITLE: Use of labeled CCK-B receptor ligands for the detection, localization, and treatment of malignant human tumors
INVENTOR(S): Reubi, Jean-Claude
PATENT ASSIGNEE(S): Mallinckrodt Medical, Inc., USA; Reubi, Jean-Claude
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9731657	A2	19970904	WO 1997-US3056	19970225
WO 9731657	A3	19971023		
W: CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
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PRIORITY APPLN. INFO.:

EP 1996-200498	A	19960227
WO 1997-US3056	W	19970225
US 1999-125823	B1	19990119

OTHER SOURCE(S): MARPAT 127:259530

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L9            1 L7 NOT PY>1998

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L9   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         1998:271563  CAPLUS
DOCUMENT NUMBER:          129:119669
TITLE:                    Unsulfated DTPA- and DOTA-CCK analogs as specific
                          high-affinity ligands for CCK-B receptor-expressing
                          human and rat tissues in vitro and in vivo
AUTHOR(S):                Reubi, J. C.; Waser, B.; Schaer, J. C.; Laederach, U.;
                          Erion, J.; Srinivasan, A.; Schmidt, M. A.; Bugaj, J.
                          E.
CORPORATE SOURCE:         Institute of Pathology, Division of Cell Biology and
                          Experimental Cancer Research, University of Berne,
                          Switz.
SOURCE:                   European Journal of Nuclear Medicine (1998), 25(5),
                          481-490
                          CODEN: EJNMD9; ISSN: 0340-6997
PUBLISHER:                Springer-Verlag
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
REFERENCE COUNT:          26    THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


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     FILE 'REGISTRY' ENTERED AT 13:36:14 ON 07 DEC 2006
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L2           424 S DYMGWMDF/SQSP

     FILE 'CAPLUS' ENTERED AT 13:39:00 ON 07 DEC 2006
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L5             5 S DOTA AND L3
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L7            12 S L6 AND L3
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L9             1 S L7 NOT PY>1998

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9844902 PY>1996
L13 20 L11 NOT PY>1996

=> d ibib 1-4

L13 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:395151 CAPLUS
DOCUMENT NUMBER: 125:133249
TITLE: The excitatory effect of cholecystokinin on rat neostriatal neurons: ionic and molecular mechanisms
AUTHOR(S): Wu, Tony; Wang, Hung-Li
CORPORATE SOURCE: Department of Neurology, Chang Gung Memorial Hospital, Kwei-San, Tao-Yuan, Taiwan
SOURCE: European Journal of Pharmacology (1996), 307(2), 125-132
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

L13 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:862980 CAPLUS
DOCUMENT NUMBER: 123:247490
TITLE: Nitric oxide modulates pepsinogen secretion induced by calcium-mediated agonist in guinea pig gastric chief cells
AUTHOR(S): Fiorucci, Stefano; Distrutti, Eleonora; Chiorean, Mihnea; Santucci, Luca; Belia, Silvia; Fano, Giorgio; De Giorgio, Roberto; Stanghellini, Vincenzo; Corinaldesi, Roberto; Morelli, Antonio
CORPORATE SOURCE: Dipartimento di Medicina Clinica, Univ. degli Studi di Perugia, Perugia, Italy
SOURCE: Gastroenterology (1995), 109(4), 1214-23
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English

L13 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:636142 CAPLUS
DOCUMENT NUMBER: 123:26032
TITLE: Potentiation of cholecystokinin-induced amylase release by peptide VIP in guinea pig pancreatic acini
AUTHOR(S): Tanaka, Keiko; Shibuya, Izumi; Kanno, Tomio
CORPORATE SOURCE: Faculty Veterinary Medicine, Hokkaido University, Sapporo, 060, Japan
SOURCE: Japanese Journal of Physiology (1995), 45(2), 241-56
CODEN: JJPHAM; ISSN: 0021-521X
PUBLISHER: Business Center for Academic Societies Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

L13 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:540954 CAPLUS
DOCUMENT NUMBER: 122:282413
TITLE: Highly sensitive non-isotopic immunoassays for cholecystokinin using various detection methods
AUTHOR(S): Ito, Katsutoshi; Kodama, Ryoko; Maeda, Masako; Tsuji, Akio
CORPORATE SOURCE: Sch. Pharmaceutical Sci., Showa Univ., Tokyo, 142, Japan
SOURCE: Analytical Letters (1995), 28(5), 797-807
CODEN: ANALBP; ISSN: 0003-2719
PUBLISHER: Dekker
DOCUMENT TYPE: Journal

LANGUAGE: English

=> d kwic

L13 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
AB . . . currents. Internal administration of heparin (2 mg/mL), an inositol 1,4,5-trisphosphate (IP3) receptor antagonist, and buffering of intracellular calcium with the Ca2+-chelator, BAPTA (1,2-bis(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid, 10 mM), suppressed CCK-8-evoked cationic currents. These findings suggest that, by activating CCKB receptors, CCK-8 excites rat. . .
IT 1947-37-1 25126-32-3, Cholecystokinin-8 (pig)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(ionic and mol. mechanisms of excitatory effect of cholecystokinin on rat neostriatal neurons)

=> s metal chelat?
1697487 METAL
855839 METALS
2059434 METAL
(METAL OR METALS)
134722 CHELAT?
L14 14458 METAL CHELAT?
(METAL(W)CHELAT?)

=> d his

(FILE 'HOME' ENTERED AT 13:35:48 ON 07 DEC 2006)

FILE 'REGISTRY' ENTERED AT 13:36:14 ON 07 DEC 2006
L1 136 S DY'NLE'GW'NLE'DF/SQSP
L2 424 S DYMGWMDF/SQSP

FILE 'CAPLUS' ENTERED AT 13:39:00 ON 07 DEC 2006
L3 84 S L1
L4 0 S DPTA AND L3
L5 5 S DOTA AND L3
L6 134722 S CHELAT?
L7 12 S L6 AND L3
L8 0 S L7 NOT PY>1997
L9 1 S L7 NOT PY>1998
L10 4485 S L2
L11 49 S L10 AND L6
L12 20 S L11 NOT PY>1997
L13 20 S L11 NOT PY>1996
L14 14458 S METAL CHELAT?

=> s l14 and l10
L15 3 L14 AND L10

=> d ibib 1-3

L15 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:271563 CAPLUS
DOCUMENT NUMBER: 129:119669
TITLE: Unsulfated DTPA- and DOTA-CCK analogs as specific high-affinity ligands for CCK-B receptor-expressing human and rat tissues in vitro and in vivo
AUTHOR(S): Reubi, J. C.; Waser, B.; Schaer, J. C.; Laederach, U.; Erion, J.; Srinivasan, A.; Schmidt, M. A.; Bugaj, J. E.
CORPORATE SOURCE: Institute of Pathology, Division of Cell Biology and

Experimental Cancer Research, University of Berne, Switz.
SOURCE: European Journal of Nuclear Medicine (1998), 25(5), 481-490
CODEN: EJNMD9; ISSN: 0340-6997
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:163822 CAPLUS
DOCUMENT NUMBER: 118:163822
TITLE: Rat kidney endopeptidase 24.16. Purification, physicochemical characteristics and differential specificity towards opiates, tachykinins and neurotensin-related peptides
AUTHOR(S): Barelli, Helene; Vincent, Jean Pierre; Checler, Frederic
CORPORATE SOURCE: Inst. Pharmacol. Mol. Cell., Univ. Nice Sophia Antipolis, Valbonne, Fr.
SOURCE: European Journal of Biochemistry (1993), 211(1-2), 79-90
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English

L15 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1981:419815 CAPLUS
DOCUMENT NUMBER: 95:19815
TITLE: Degradation of cholecystokinin-like peptides by a crude rat brain synaptosomal fraction: a study by high pressure liquid chromatography
AUTHOR(S): Deschodt-Lanckman, Monique; Bui, Ngoc Diem; Noyer, Michel; Christophe, Jean
CORPORATE SOURCE: Med. Sch., Univ. Libre Bruxelles, Brussels, B-1000, Belg.
SOURCE: Regulatory Peptides (1981), 2(1), 15-30
CODEN: REPPDY; ISSN: 0167-0115
DOCUMENT TYPE: Journal
LANGUAGE: English

=> d ibib kwic 2-3

L15 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:163822 CAPLUS
DOCUMENT NUMBER: 118:163822
TITLE: Rat kidney endopeptidase 24.16. Purification, physicochemical characteristics and differential specificity towards opiates, tachykinins and neurotensin-related peptides
AUTHOR(S): Barelli, Helene; Vincent, Jean Pierre; Checler, Frederic
CORPORATE SOURCE: Inst. Pharmacol. Mol. Cell., Univ. Nice Sophia Antipolis, Valbonne, Fr.
SOURCE: European Journal of Biochemistry (1993), 211(1-2), 79-90
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Endopeptidase 24.16 was purified from rat kidney homogenate on the basis of its ability to generate the biol. inactive degradation products neurotensin (1-10) and neurotensin (11-13). On SDS gels of the proteins pooled after

the last purification step, the enzyme appeared homogeneous and behaved as a 70-kDa monomer. The peptidase was not sensitive to specific inhibitors of aminopeptidases, pyroglutamyl aminopeptidase I, endopeptidase 24.11, endopeptidase 24.15, proline endopeptidase and angiotensin-converting enzyme but was potently inhibited by several metal chelators such as o-phenanthroline and EDTA and was blocked by divalent cations. The specificity of endopeptidase 24.16 towards peptides of the tachykinin, opioid and neurotensin families was examined by competition expts. of tritiated neurotensin hydrolysis as well as HPLC anal. These results indicated that endopeptidase 24.16 could discriminate between peptides belonging to the same family. Neurotensin, Lys8-Asn9-neurotensin(8-13) and xenopsin were efficiently hydrolyzed while neuromedin N and kinetensin underwent little if any proteolysis by the peptidase. Analogously, substance P and dynorphins (1-7) and (1-8) were readily proteolyzed by endopeptidase 24.16 while neurokinin A, amphibian tachykinins and leucine or methionine enkephalins totally resisted degradation By Triton X-114 phase separation, 15-20% of endopeptidase 24.16 partitioned in the detergent phase, indicating that renal endopeptidase 24.16 might exist in a genuine membrane-bound form. The equipotent solubilization of the enzyme by 7 detergents of various critical micellar concns. confirmed the occurrence of a membrane-bound counterpart of endopeptidase 24.16. Furthermore, the absence of release elicited by phosphatidylinositol-specific phospholipase C suggested that the enzyme was not attached by a glycosyl-phosphatidylinositol anchor in the membrane of renal microvilli. Finally, endopeptidase 24.16 could not be released from these membranes upon trypsinolysis.

IT 50-56-6, Oxytocin, biological studies 69-25-0, Eledoisin 113-79-1, [Arg8]vasopressin 2507-24-6, Physalaemin 9034-40-6, LHRH 24305-27-9, TRH 25126-32-3 31362-50-2, Bombesin 33507-63-0, Substance P 37213-49-3, α-Melanotropin 63968-82-1, Kassinin 86933-74-6, Neurokinin A 86933-75-7
RL: BIOL (Biological study)
(endopeptidase 24.16 of kidney microvillus specificity for)

L15 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1981:419815 CAPLUS
DOCUMENT NUMBER: 95:19815
TITLE: Degradation of cholecystokinin-like peptides by a crude rat brain synaptosomal fraction: a study by high pressure liquid chromatography
AUTHOR(S): Deschodt-Lanckman, Monique; Bui, Ngoc Diem; Noyer, Michel; Christophe, Jean
CORPORATE SOURCE: Med. Sch., Univ. Libre Bruxelles, Brussels, B-1000, Belg.
SOURCE: Regulatory Peptides (1981), 2(1), 15-30
CODEN: REPPDY; ISSN: 0167-0115
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Degradation of cholecystokinin-8 (CK-8), CCK-4, and related peptides by a crude synaptosomal fraction of rat brain was investigated by monitoring the tryptophan fluorescence of reaction products after HPLC fractionation. At 20°, the half disappearance time was 52 min for CCK-8, 35 min for unsulfated CCK-8, 20 min for unsulfated CCK-7, 6 min for Tyr(SO3H)-Trp-Met-Asp-Phe-NH2, and 3 min only for CCK-4. Caerulein was much more resistant than CCK-8, and Boc-CCK-4 (where Boc = tert-butoxycarbonyl) and Aoc-CCK-4 (where Aoc = tert-amyloxycarbonyl) remained stable for ≥3 h. The apparent Km for CCK-8 and CCK-4 was 40 μM and maximal activity on CCK-8 was observed at pH 7.0. Zn2+ was strongly inhibitory. The protease inhibitors puromycin and bacitracin, the metal chelator 1,10-phenanthroline, and the SH blocking agents N-ethylmaleimide and p-chloromerlcuribenzoate greatly reduced the release of tryptophan from CCK-8. Puromycin inhibition of CCK-8 degradation provoked the accumulation of a CCK-7-like peptide, and that of CCK-4 degradation was of a competitive type (Ki = 2 μM). The CCK-8-degrading activity of brain synaptosomes was present in the cytosol

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9731657	A2	19970904	WO 1997-US3056		19970225
WO 9731657	A3	19971023			
W: CA, JP, US					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
CA 2247430	AA	19970904	CA 1997-2247430		19970225
EP 885017	A2	19981223	EP 1997-908751		19970225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2000506141	T2	20000523	JP 1997-531108		19970225
US 2004185510	A1	20040923	US 2003-626229		20030724
PRIORITY APPLN. INFO.:			EP 1996-200498	A	19960227
			WO 1997-US3056	W	19970225
			US 1999-125823	B1	19990119

OTHER SOURCE(S): MARPAT 127:259530

L17 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:69756 CAPLUS
DOCUMENT NUMBER: 110:69756
TITLE: Effects of cholecystokinin-octapeptide (CCK-8) on food intake and gastric emptying in man
AUTHOR(S): Muurahainen, Norma; Kissileff, Harry R.; Derogatis, Andrew J.; Xavier Pi Sunyer, F.
CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, 10025, USA
SOURCE: Physiology & Behavior (1988), 44(4-5), 645-9
CODEN: PHBHA4; ISSN: 0031-9384
DOCUMENT TYPE: Journal
LANGUAGE: English

=> d kwic 9

L17 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
AB . . . infusions of CCK-8 and saline on sep. nonconsecutive days after they had consumed 500 g of tomato soup tagged with technetium-99-DTPA. Intake of a test meal was measured 20 min after consumption of the soup whereas gastric emptying was simultaneously monitored. . .
IT 25126-32-3
RL: BIOL (Biological study)
(appetite and stomach emptying response to, in man)

=> file dissab

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	69.02	128.33

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.00	-3.00

FILE 'DISSABS' ENTERED AT 13:46:43 ON 07 DEC 2006

FILE COVERS 1861 TO 27 NOV 2006 (20061127/ED)

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```
=> s cholecystokinin or (CCK-8 or CCK8 or CCK () 8))
UNMATCHED RIGHT PARENTHESIS '8))'
The number of right parentheses in a query must be equal to the
number of left parentheses.

=> s cholecystokinin or (CCK-8 or CCK8 or (CCK () 8))
          307 CHOLECYSTOKININ
          299 CCK
            1 CCKS
          299 CCK
                (CCK OR CCKS)
        85654 8
           65 CCK-8
                (CCK(W)8)
           13 CCK8
          299 CCK
            1 CCKS
          299 CCK
                (CCK OR CCKS)
        85654 8
           65 CCK (W) 8
L18       323 CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK (W) 8))

=> s DTPA or DOTA
          330 DTPA
           38 DOTA
L19       360 DTPA OR DOTA

=> s l19 and l18
L20         2 L19 AND L18

=> d ibib 1-2

L20  ANSWER 1 OF 2  DISSABS COPYRIGHT (C) 2006 ProQuest Information and
     Learning Company; All Rights Reserved on STN
ACCESSION NUMBER:   96:28812  DISSABS   Order Number: AAIMM03308
TITLE:              POLYAMINOPOLYCARBOXYLIC ACIDS FOR RADIOLABELLING SMALL
                    DRUGS
AUTHOR:             BARLOW, STEPHEN ROBERT [M.SC.]; HUNTER, DUNCAN H. [advisor]
CORPORATE SOURCE:   THE UNIVERSITY OF WESTERN ONTARIO (CANADA) (0784)
SOURCE:             Masters Abstracts International, (1995) Vol. 34, No. 3, p.
                    1181. Order No.: AAIMM03308. 137 pages.
                    ISBN: 0-612-03308-2.
DOCUMENT TYPE:      Dissertation
FILE SEGMENT:       MAI
LANGUAGE:           English
ENTRY DATE:         Entered STN: 19960708
                    Last Updated on STN: 19960708

L20  ANSWER 2 OF 2  DISSABS COPYRIGHT (C) 2006 ProQuest Information and
     Learning Company; All Rights Reserved on STN
ACCESSION NUMBER:   95:14070  DISSABS   Order Number: AARC391489 (not available
                    for sale by UMI)
TITLE:              ENDOGENOUS CHOLECYSTOKININ MODULATES GASTRIC
                    EMPTYING AND POSTPRANDIAL RELEASE OF INSULIN IN HUMANS
                    INFLUENCIA DE LA COLECISTOKININA ENDOGENA EN EL VACIAMIENTO
                    GASTRICO Y EN LA SECRECION POSPRANDIAL DE INSULINA EN EL
```

```
                    HOMBRE
AUTHOR:             HIDALGO GRAU, LUIS ANTONIO
CORPORATE SOURCE:   UNIVERSITAT AUTONOMA DE BARCELONA (SPAIN) (5852)
SOURCE:             Dissertation Abstracts International, (1993) Vol. 56, No.
                    1C, p. 157. Order No.: AARC391489 (not available for sale
                    by UMI). SERVEI DE PUBLICACIONS DE LA UNIVERSITAT AUTONOMA
                    DE BARCELONA, EDIFICI  RECTORAT, APARTAT POSTAL 20, E-08193
                    BELLATERRA (BARCELONA), SPAIN.
                    ISBN: 84-7929-812-X.
DOCUMENT TYPE:      Dissertation
FILE SEGMENT:       DAI
LANGUAGE:           Spanish
ENTRY DATE:         Entered STN: 19950321
                    Last Updated on STN: 19950321


=> d kwic 1-2

L20  ANSWER 1 OF 2  DISSABS COPYRIGHT (C) 2006 ProQuest Information and
     Learning Company; All Rights Reserved on STN
AB        . . .  of radioisotopes for physiological studies. Their use for
     the labelling of small compounds such as drugs has not been reported.
           Cholecystokinin (CCK) is a hormone whose actions have been
     associated with satiety, and whose levels have been found to be abnormal.
     . .  $\sp{111}$In or $\rm \sp{99m}$Tc using polyaminopolycarboxylic acid
     chelators is reported. The synthesis of disubstituted as opposed to
     monosubstituted EDTA and DTPA resulted from reaction of a model
     amine with the dianhydrides of EDTA and DTPA under various
     reaction conditions.

L20  ANSWER 2 OF 2  DISSABS COPYRIGHT (C) 2006 ProQuest Information and
     Learning Company; All Rights Reserved on STN
TI   ENDOGENOUS CHOLECYSTOKININ MODULATES GASTRIC EMPTYING AND
     POSTPRANDIAL RELEASE OF INSULIN IN HUMANS
     INFLUENCIA DE LA COLECISTOKININA ENDOGENA EN EL VACIAMIENTO GASTRICO Y.
     .
AB        Aim of the study. To determine the effect of endogenous
     cholecystokinin (CCK) on gastric emptying and postprandial release
     of insulin in humans.
          Materials and method. Six healthy volunteers underwent three
     experiments..  . .  liquid meal containing 100 g glucose, and an egg yolk
     mixed with 150 ml of milk. To evaluate gastric emptying, Tc99-DTPA
     (2 mCu) was added to the meal. To evaluate gallbladder emptying, Tc99-HIDA
     (5 mCu) was given i.v. one hour before.  . .


=> s metal chelat?
         34727 METAL
         11101 METALS
         40243 METAL
                 (METAL OR METALS)
          4454 CHELAT?
L21        497 METAL CHELAT?
                 (METAL(W)CHELAT?)

=> d his

     (FILE 'HOME' ENTERED AT 13:35:48 ON 07 DEC 2006)

     FILE 'REGISTRY' ENTERED AT 13:36:14 ON 07 DEC 2006
L1           136 S DY'NLE'GW'NLE'DF/SQSP
L2           424 S DYMGWMDF/SQSP

     FILE 'CAPLUS' ENTERED AT 13:39:00 ON 07 DEC 2006
L3            84 S L1
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L4             0 S DPTA AND L3
L5             5 S DOTA AND L3
L6        134722 S CHELAT?
L7            12 S L6 AND L3
L8             0 S L7 NOT PY>1997
L9             1 S L7 NOT PY>1998
L10         4485 S L2
L11           49 S L10 AND L6
L12           20 S L11 NOT PY>1997
L13           20 S L11 NOT PY>1996
L14        14458 S METAL CHELAT?
L15            3 S L14 AND L10
L16            4 S L10 AND (DPTA OR DOTA)
L17            9 S L10 AND DTPA

     FILE 'DISSABS' ENTERED AT 13:46:43 ON 07 DEC 2006
L18          323 S CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK () 8))
L19          360 S DTPA OR DOTA
L20            2 S L19 AND L18
L21          497 S METAL CHELAT?

=> s l21 and l18
L22            0 L21 AND L18

=> file pctfull
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     7.67     136.00

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00      -3.00

FILE 'PCTFULL' ENTERED AT 13:50:53 ON 07 DEC 2006
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FILE LAST UPDATED:          5 DEC 2006      <20061205/UP>
MOST RECENT UPDATE WEEK:       200648        <200648/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

>>> NEW IPC8 DATA AND FUNCTIONALITY NOW AVAILABLE IN THIS FILE.
    SEE
    http://www.stn-international.de/stndatabases/details/ipc-reform.html >>>

>>> FOR CHANGES IN PCTFULL PLEASE SEE HELP CHANGE
    (last updated April 10, 2006) <<<

=> s cholecystokinin or (CCK-8 or CCK8 or (CCK () 8))
          1899 CHOLECYSTOKININ
           132 CHOLECYSTOKININS
          1949 CHOLECYSTOKININ
                 (CHOLECYSTOKININ OR CHOLECYSTOKININS)
          2003 CCK
            36 CCKS
          2007 CCK
                 (CCK OR CCKS)
       1002744 8
           255 CCK-8
                 (CCK(W)8)
            63 CCK8
          2003 CCK
            36 CCKS
          2007 CCK
```

```
                (CCK OR CCKS)
       1002744 8
           255 CCK (W) 8
L23       2006 CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK (W) 8))

=> s DPTA or DOTA
           910 DPTA
             1 DPTAS
           910 DPTA
                 (DPTA OR DPTAS)
          1767 DOTA
             5 DOTAS
          1768 DOTA
                 (DOTA OR DOTAS)
L24       2224 DPTA OR DOTA

=> s DTPA or DOTA
          5576 DTPA
            12 DTPAS
          5579 DTPA
                 (DTPA OR DTPAS)
          1767 DOTA
             5 DOTAS
          1768 DOTA
                 (DOTA OR DOTAS)
L25       6121 DTPA OR DOTA

=> s l25 and l23
L26        110 L25 AND L23

=> s l26 not py>1996
        935225 PY>1996
L27         10 L26 NOT PY>1996

=> d ibib 1-10

L27    ANSWER 1 OF 10    PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:       2001076631 PCTFULL
       no bibliographic data available - please use FPI for PI information
DESIGNATED STATES

L27    ANSWER 2 OF 10    PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:       1996040293 PCTFULL  ED 20020514
TITLE (ENGLISH):        STRUCTURALLY DETERMINED METALLO-CONSTRUCTS AND
                        APPLICATIONS
TITLE (FRENCH):         METALLO-ASSEMBLAGES DETERMINES STRUCTURALEMENT ET
                        APPLICATIONS
INVENTOR(S):            SHARMA, Shubh, D.
PATENT ASSIGNEE(S):     RHOMED INCORPORATED;
                        SHARMA, Shubh, D.
LANGUAGE OF PUBL.:      English
DOCUMENT TYPE:          Patent
PATENT INFORMATION:
                        NUMBER              KIND     DATE
                        ---------------------------------
                        WO 9640293            A1 19961219
DESIGNATED STATES
       W:               AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI
                        GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD
                        MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM
                        TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ
                        MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC
                        NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.:      WO 1996-US9840        A  19960606
PRIORITY INFO.:         US 1995-8/476,652        19950607
```

US 1996-8/660,697 19960605

L27 ANSWER 3 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1996039128 PCTFULL ED 20020514
TITLE (ENGLISH): PROTEIN PARTICLES FOR THERAPEUTIC AND DIAGNOSTIC USE
TITLE (FRENCH): PARTICULES PROTEIQUES A USAGE THERAPEUTIQUE ET DIAGNOSTIQUE
INVENTOR(S): YEN, Richard, C., K.
PATENT ASSIGNEE(S): HEMOSPHERE, INC.;
YEN, Richard, C., K.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9639128	A1	19961212

DESIGNATED STATES
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1996-US9458	A	19960604
PRIORITY INFO.:	US 1995-8/471,650		19950606
	US 1995-8/554,919		19951109

L27 ANSWER 4 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995015118 PCTFULL ED 20020514
TITLE (ENGLISH): GAS MICROSPHERES FOR TOPICAL AND SUBCUTANEOUS APPLICATION
TITLE (FRENCH): MICROSPHERES GAZEUSES POUR APPLICATION TOPIQUE ET SOUS-CUTANEE
INVENTOR(S): UNGER, Evan, C.;
MATSUNAGA, Terry;
YELLOWHAIR, David
PATENT ASSIGNEE(S): UNGER, Evan, C.;
MATSUNAGA, Terry;
YELLOWHAIR, David
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9515118	A1	19950608

DESIGNATED STATES
W: AU CA CN JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.:	WO 1994-US13817	A	19941130
PRIORITY INFO.:	US 1993-8/159,674		19931130
	US 1993-8/159,687		19931130
	US 1993-8/160,232		19931130
	US 1994-8/307,305		19940916
	US 1994-8/346,426		19941129

L27 ANSWER 5 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995005842 PCTFULL ED 20020514
TITLE (ENGLISH): METHOD AND DEVICE FOR TREATING GASTROINTESTINAL MUSCLE DISORDERS AND OTHER SMOOTH MUSCLE DYSFUNCTION
TITLE (FRENCH): PROCEDE ET DISPOSITIF POUR TRAITER LES TROUBLES MUSCULAIRES GASTRO-INTESTINAUX ET AUTRES DYSFONCTIONNEMENTS DES MUSCLES LISSES
INVENTOR(S): PASRICHA, Pankaj, J.;
KALLOO, Anthony, N.
PATENT ASSIGNEE(S): THE JOHNS HOPKINS UNIVERSITY

DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9505842	A1	19950302

DESIGNATED STATES
W: CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1994-US9759 A 19940823
PRIORITY INFO.: US 1993-112,088 19930826

L27 ANSWER 6 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1994004674 PCTFULL ED 20020513
TITLE (ENGLISH): HUMAN MELANOCYTE STIMULATING HORMONE RECEPTOR
TITLE (FRENCH): RECEPTEUR D'HORMONE STIMULANT LE MELANOCYTE CHEZ L'HOMME
INVENTOR(S): WIKBERG, Jarl;
CHHAJLANI, Vijay
PATENT ASSIGNEE(S): WIKBERG, Jarl;
CHHAJLANI, Vijay
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9404674	A1	19940303

DESIGNATED STATES
W: AU BB BG BR BY CA CZ FI HU JP KP KR KZ LK MG MN MW NO NZ PL RO RU SD SK UA US VN AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.: WO 1993-DK273 A 19930820
PRIORITY INFO.: DK 1992-1046/92 19920821
DK 1992-1118/92 19920910
DK 1993-528/93 19930505

L27 ANSWER 7 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1993018797 PCTFULL ED 20020513
TITLE (ENGLISH): METHOD OF INTRAOPERATIVELY DETECTING AND LOCATING TUMORAL TISSUES
TITLE (FRENCH): PROCEDE POUR DETECTER ET LOCALISER DE FACON PEROPERATOIRE DES TISSUS TUMORAUX
INVENTOR(S): ENSING, Geert, Jacob;
PANEK, Karel, Jan;
DOEDENS, Bareld, Jan
PATENT ASSIGNEE(S): MALLINCKRODT MEDICAL, INC.;
ENSING, Geert, Jacob;
PANEK, Karel, Jan;
DOEDENS, Bareld, Jan
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9318797	A1	19930930

DESIGNATED STATES
W: AU CA JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1993-US2772 A 19930324
PRIORITY INFO.: NL 1992-92200848.7 19920325

L27 ANSWER 8 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1992004916 PCTFULL ED 20020513
TITLE (ENGLISH): PARTICULATE AGENTS
TITLE (FRENCH): AGENTS SOUS FORME DE PARTICULES
INVENTOR(S): FILLER, Aaron, Gershon

PATENT ASSIGNEE(S): ST. GEORGE'S ENTERPRISES LIMITED;
FILLER, Aaron, Gershon
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9204916	A2	19920402

DESIGNATED STATES
W: AT AU BE CA CH DE DK ES FR GB GR IT JP LU NL NO SE US

APPLICATION INFO.:	WO 1991-EP1780	A	19910913
PRIORITY INFO.:	GB 1990-9020075.9		19900914
	GB 1990-9023580.5		19901030
	GB 1990-9027293.1		19901217
	GB 1991-9100233.7		19910107
	GB 1991-9100981.1		19910116
	GB 1991-9102146.9		19910131
	GB 1991-9110876.1		19910520
	GB 1991-9116373.3		19910730
	GB 1991-9117851.7		19910819
	GB 1991-9118676.7		19910830

L27 ANSWER 9 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1992001469 PCTFULL ED 20020513
TITLE (ENGLISH): A COMPOSITION PROVIDING IMPROVED CLEARANCE OF BIOACTIVE SUBSTANCES FROM THE BLOODSTREAM
TITLE (FRENCH): COMPOSITION ASSURANT UNE MEILLEURE ELIMINATION DE SUBSTANCES BIOACTIVES CONTENUES DANS LE SYSTEME SANGUIN
INVENTOR(S): SELMER, Johan
PATENT ASSIGNEE(S): NOVO NORDISK A/S;
SELMER, Johan
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9201469	A1	19920206

DESIGNATED STATES
W: AT AU BE CA CH CS DE DK ES FI FR GB GR HU IT JP KR LU NL NO PL SE SU US

APPLICATION INFO.:	WO 1991-DK215	A	19910724
PRIORITY INFO.:	DK 1990-1762/90		19900724

L27 ANSWER 10 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1989009625 PCTFULL ED 20020513
TITLE (ENGLISH): CONTRAST AGENTS FOR MAGNETIC RESONANCE IMAGING
TITLE (FRENCH): AMELIORATIONS APPORTEES A L'IMAGERIE PAR RESONANCE MAGNETIQUE
INVENTOR(S): BERG, Arne;
KLAVENESS, Jo
PATENT ASSIGNEE(S): COCKBAIN, Julian, Roderick, Michaelson;
NYCOMED AS;
BERG, Arne;
KLAVENESS, Jo
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 8909625	A1	19891019

DESIGNATED STATES
W: AT AU BE CH DE DK FI FR GB IT JP LU NL NO SE US

APPLICATION INFO.:	WO 1989-EP376	A	19890406
PRIORITY INFO.:	GB 1988-8808305.0		19880408

=> d kwic 10

L27 ANSWER 10 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN

DETD . . . use of paramagnetic
metal chelates, for example of aminopolycarboxylic
acids such as nitrilotriacetic acid (NTA)jjNrNrN1rN'-
ethylenediaminetetraacetic acid (EDTA), N-hydroxyethyl-
-N,N1,N1-ethylenediaminetriacetic acid (HEDTA)r NrNrN'r-
N'',N''-diethylenetriaminepentaacetic acid (DTPA),
and 1,4,7,10-tetraazacyclododecanetetraacetic acid
(DOTA) (see for example EP-A-71564, EP-A-130934t
DE-A-3401052 and US-A-4639365). and Nycomed AS have
suggested the use of paramagnetic metal chelates
of iminodiacetic acids (see. . .

Intravenous administration, at separate timesf of
the positive contrast agent Gd DTPA-dimeglumine (which
following such administration rapidly distributes
extracellularly) and of superparamagnetic ferrite
particles was proposed by Weissleder et al.'in AJR
150: 561-566 (1988) for imaging. . .

. . .
the reticuloendothelial system targetting
negative contrast agents of W085/04330. However,,
extracellularly distributing paramagnetic metal containing
positive contrast agents, such as Gd DTPAF Gd DOTA
and Od DTPA-BMA (the gadolinium chelate of the bismethylamide
of DTPA), may be used according to the present invention
for administration into body cavities or tracts having
externally voiding ducts, e.g. for oral. . .

. . .
metal
chelates in which the paramagnetic metal species
+ 3+ especially Dy 3+ are particularly
is Tb or Sm or more
preferred, eag, Dy DTPA-BMAr, or DyDTPA-beta-alanine-
dextran (molecular weight 70000) where a blood pooling
positive contrast agent is desired.

EDTA; DTPA-BMA; DOTA; desferrioxamine; and the
physiologically
acceptable salts thereof.

. . .
contrast agent,
if uniform distribution after i.v. administration
is desired, one may conveniently use as the chelating
moiety a hydrophilic extracellular substance, such
as DTPA or DOTA or a chelating agent as claimed in
W089/00557. However, to achieve tissue- or duct-
specificity, for either positive or negative MRI
contrast agents. . .

. . .
the same equipment against
distilled water to a volume of 1150 ml, the pH-
was adjusted to 9 with N-methylmorpholine and 29.18g
of DTPA-bis-anhydride was added while the pH was
kept at 8 using the same base. When the solution
became clear, the reaction mixture was. . .

Gd 4.6%; N 2.15%; Na 0.16%; Cl less than 0101%,
1
Free Gd (xylene orange titration), DTPA, GdDTPA?
citric acid, or DMSO (HPLC): less than 0.01%

(The percentages in the analysis results are by weight).

in three of the dogs to which the positive and negative contrast agents were administered, 1.0 unit/kg bodyweight of cholecystokinin were given intravenously 60 minutes after administration of the paramagnetic contrast agent immediately followed by examinations in the transverse and frontal projections.

. . .

gall bladder was also encountered 15 to 30 minutes after contrast agent administration. After administration of the superparamagnetic and paramagnetic contrast agents and after cholecystokinin injection, the gall bladder was moderately contracted and visualization of the choledocus duct was achieved as well as contrast filling of the duodenum.

=> d ibib kwic 1-9

L27 ANSWER 1 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 2001076631 PCTFULL
no bibliographic data available - please use FPI for PI information
DESIGNATED STATES

DETD 37(4):449-57 [1997]; McHugh, PR. and Moran, TH., The stomach, cholecystokinin, and satiety, Fed. Proc. 45(5):13 84-90 [1986]; Lin, H.C. et al., Frequency ofgastric pacesetter potential depends on volume and site of distension,. . .

There may also be some interactions between 5-HT receptor-mediated effects and cholecystokinin-mediated effects on satiety. (Voight, J.P. et al., Evidencefor the involvement of the 5-HTIA receptor in CKK induced satiety in rats, Nauyn Schmiedebergs Arch. Pharmacol. 351(3):217-20 [1995]; Varga, G. et al., Effect of deramciclane, a new 5-HT receptor antagonist, on cholecystokinin -induced changes in ratgastrointesfinalfunction, Eur. J. Pharrnacol. 367(2-3):315-23 [1999]; but see, Eberle-Wang, K. and Simansky, K.J., Yhe CKK-A receptor antagonist, devazepide, blocks. . .

2 o Behav. 43(3):943-47 [1992]). The neuropeptide hormone cholecystokinin is known to induce satiety, inhibit gastric emptying, and to stimulate digestive pancreatic and gall bladder activity. (Blevins, J.E. et al., Brain regions where cholecystokinin suppresses feeding in rats, Brain Res. 860(1-2):1-10 [2000]; Moran, TH. and McHugh, P.R., Cholecystokinin suppressesfood intake by inhibiting gastric emptying, Am. J. Physiol.

Cholecystokinin, and other neuropeptides, such as bombesin, arnylin, proopiomelanocortin, corticoptropin-releasing factor, galanin, melanin-concentrating hormone, neurotensin, agouti-related protein, leptin, and neuropeptide Y, are important 3. . .

. . .
(preferred dose range of 0 5 mg/kg), deramciclane (Varga,
G. et al., Effect of deramciclane, a new 5-HT receptor antagonist, on
cholecystokinin-
1 0 induced changes in rat gastrointestinalfunction, Eur. J. Pharmacol.
367(2-3):315-23
[1999]), or alosetron. 5-HT4 receptor antagonists are preferably used at
a. . .
. . .
0 with phosphate buffer, pH 7.0, at 2 mL/min. 60 minutes after the start
of the perfusion,
5 1
-20 [Xi of Tc-DTPA (diethylenetlianiinepentaacetic acid) was
delivered as a bolus into
the test segment. Intestinal transit was then measured by counting the
radioactivity of. . .
. . .
liquid marker across the approximately 150 cm intestinal test segment by
delivering
about 20 gCi 'Tc chelated to diethyltriamine pentaacetic acid (
DTPA)(Cunningham,
K.M. et al., Use of technicium-99m (V)thiocyanate to measure gastric
emptying offat,
J. Nucl. Med. 32:878-881 [1991]) as a bolus into the. . . gamma well
counter. After correcting
all counts to time zero, intestinal transit was calculated as the
cumulative percent recovery
of the delivered Tc-DTPA. This method has been well validated
over the years and
appreciated for its advantage of minimal inadvertent marker loss. To
demonstrate. . .

L27 ANSWER 2 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1996040293 PCTFULL ED 20020514
TITLE (ENGLISH): STRUCTURALLY DETERMINED METALLO-CONSTRUCTS AND APPLICATIONS
TITLE (FRENCH): METALLO-ASSEMBLAGES DETERMINES STRUCTURALEMENT ET APPLICATIONS
INVENTOR(S): SHARMA, Shubh, D.
PATENT ASSIGNEE(S): RHOMED INCORPORATED;
SHARMA, Shubh, D.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9640293	A1	19961219

DESIGNATED STATES
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI
GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD
MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM
TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ
MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC
NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1996-US9840	A	19960606
PRIORITY INFO.:	US 1995-8/476,652		19950607
	US 1996-8/660,697		19960605

DETD . . . or Cu., to an equirnolar covalent
adduct of diethylenetriaminepentaacetic acid (DT?A) with
ethylenediamine. This adduct
may be achieved by reacting ethylenediamine with DTPA
-dianhydride. The amino group
of the ethylenediamine moiety in this adduct, together with the free
carboxylate of the DTPA

moiety, mimic the two primary integrin receptor-binding functionalities. The use of higher
hornologues of ethylenediarnine, or use of other di-amines, such as. . .
. . .
a reversed turn structure as their hypothesized biologically active structure. The
exan3ples of these include various peptide hormones such as somatostatin, cholecystokinin,
opioid peptides, melanotropins, luteinizing hormone releasing hormone, tachykinins and
various antibody epitopes.

L27 ANSWER 3 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1996039128 PCTFULL ED 20020514
TITLE (ENGLISH): PROTEIN PARTICLES FOR THERAPEUTIC AND DIAGNOSTIC USE
TITLE (FRENCH): PARTICULES PROTEIQUES A USAGE THERAPEUTIQUE ET DIAGNOSTIQUE
INVENTOR(S): YEN, Richard, C., K.
PATENT ASSIGNEE(S): HEMOSPHERE, INC.;
YEN, Richard, C., K.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9639128	A1	19961212

DESIGNATED STATES
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1996-US9458	A	19960604
PRIORITY INFO.:	US 1995-8/471,650		19950606
	US 1995-8/554,919		19951109

DETD . . . factor beta
receptor
14. anti-beta-lipoprotein
15. alpha 2-macroglobulin
16. streptokinase
17. anti-progesterone antibody
18. anti-leukotriene B4 antibody
19. CGGRGDF-NH2
20. doxorubicin
21. daunarubicin
22. EDTA-conjugated to HSA
23. DTPA-conjugated to HSA
24. technetium
25. gadolinium
26. HSA conjugated to FITC (Fluorescein Isothiocyanate)
27. HSA conjugated to TRITC (Tetramethylrhodamine B isothiocyanate)
28. HSA conjugated to. . . Tc99m can be achieved through direct covalent bonding or through a chelating agent. Examples of chelating agents are cysteine-cyclohexanol conjugate and DTPA

Biologically active peptides:
myl-L-Ala-D-Glu Amide
N-Acetyl-Asp-Glu
42

N-Acetyl-Cholecystokinin and its fragments
N-Acetyl-Hirudin and its fragments
Acetyl-Leu-Leu-Argininal
N-Acetyl-Leu-Leu-Methioninal
N-Acetyl-Leu-Leu-Norleucinal
Acetyl-Met-Asp-Arg-Val-Leu-Ser-Arg-Tyr
N-Acetyl-Met-Leu-Phe
N-Acetylmuramyl-D-alanyl-D-isoglutamine
N-Acetylmuramyl-L-alanyl-D-isoglutamine
N-Acetylmuramyl-L-alanyl-L-isoglutamine
N-Acetylmuramyl-Ala-D-isoglutaminyl-Ne-stearoyl-Lys
N-Acetyl-Phe-Nle-Arg-Phe Amide
Acetyl-Renin Substrate Tetradecapeptide
Acetyl-Ser-Asp-Lys-Pro
Acetyl-Ser-Gln-Asn-Tyr
Acetyl-Ser-Gln-Asn-Tyr-Pro-Val-Val Amide. . .
Carassin
N-Carboxymethyl-Phe-Leu
Cardioexcitatory Peptide
45
alpha-Casein and fragments
Beta-Casomorphin
Na-CBZ-Arg-Arg-Pro-Phe-His-Sta-Ile-His-Ne-BOC-Lys Methyl Ester
l Ester
CBZ-Leu-Val-Gly Diazomethyl Ketone
N-CBZ-D-Phe-Phe-Gly
N-CBZ-Pro-D-Leu
N-CBZ-Pro-Leu-Gly Hydroxamate
CD4 and fragments
Cecropins
Cerebellin
Chemostactic Peptides
Cholecystokinin and fragments
Chorionic Gonadotropin and fragments
Chromostatin-20
Chymostatin
Circumsporozoite (CS) Protein of Plasmodium falciparum
repetitive sequences
Collagen
Conotoxin GI
A-conotoxin GIIIB
w-conotoxin GVIA
a-conotoxin SI
Copper. . .
.
NITR7, DM-nitrophen, NITRS/AM; Ammonium N-
nitrosophenyl-hydroxylamine; Ammonium purpurate;
alpha-Benzoin oxime; N, N-Bis-(hydroxyethyl)-glycine;
2,3-butane-dione dioxime; Trans-1,2-Diaminocyclo-
hexanetetra-acetic acid (CDTA); Diethylene-
triaminopenta-acetic acid (DTPA); 4,5-Dihydroxy-
benzene-1,3-disulphonic acid; 2,3-Dimercapto-1-
60
Propanol; Diphenylthio-carbazone; 2,2'-Dipyridyl;
3,6-Disulpho-1,8-dihydroxy-naphthalene;
Dithiooxamide; Eriochrome Black T; Ethylene-diamine;
Ethylenediaminetetraacetic acid (EDTA); (Ethylene-
dioxy)-diethylenedinitrilo-tetraacetic acid (EGTA);
o-Hydroxybenzaldehyde. . .

L27 ANSWER 4 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995015118 PCTFULL ED 20020514
TITLE (ENGLISH): GAS MICROSPHERES FOR TOPICAL AND SUBCUTANEOUS APPLICATION
TITLE (FRENCH): MICROSPHERES GAZEUSES POUR APPLICATION TOPIQUE ET

SOUS-CUTANEE

INVENTOR(S): UNGER, Evan, C.;
MATSUNAGA, Terry;
YELLOWHAIR, David

PATENT ASSIGNEE(S): UNGER, Evan, C.;
MATSUNAGA, Terry;
YELLOWHAIR, David

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9515118	A1	19950608

DESIGNATED STATES
W: AU CA CN JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.:	WO 1994-US13817	A	19941130
PRIORITY INFO.:	US 1993-8/159,674		19931130
	US 1993-8/159,687		19931130
	US 1993-8/160,232		19931130
	US 1994-8/307,305		19940916
	US 1994-8/346,426		19941129

DETD . . . of topical or subcutaneous application and delivery: melanin concentrating hormone,, melanin stimulating hormone, trypsin inhibitor, Bowman Burk inhibitor, luteinizing hormone releasing hormone (LHRH), bombesin, cholecystokinin, insulin, gastrin, endorphins, enkephalins, growth hormone, prolactin, oxytocin, follicle stimulating hormone (FSH), human chorionic gonadotropin,, corticotropin, 0 and lipotropin, calcitonin, glucagon, thyrotropin, elastin, cyclosporin,. . .

Suitable chelants and chelating agents include, but are not limited to: penicillamine; citrate; ascorbate; diethylenetriaminepentaacetic acid (DTPA), and derivatives and salts thereof; dihydroxypropylethylenediamine (DPEA), and derivatives and salts thereof; cyclohexanediaminetetraacetic acid (CHTA), and derivatives and salts thereof; ethylenediaminetetraacetic acid (EDTA), and. . . thereof; N,Nf-(1,2-ethanedivinylbis(oxy-2,1-phenylene))bis(N-(carboxymethyl) (BAPTA), and derivatives and salts thereof; aminophenol-triacetic acid (APTRA), and derivatives and salts thereof; tetrakis(2-pyridylmethyl)ethylenediamine (TPEN), and derivatives and salts thereof; 1.4,7,10-tetraazacyclodecane (DOTA) and derivatives and salts thereof; and cyanins and their derivatives,
Furthermore, immunosuppressants or anti-inflammatory preparations can be incorporated into the gas and gaseous. . .

These metal ions may be incorporated into the microspheres as free salts, as complexes, e,g., with EDTA, DTPA, DOTA or
desferrioxamine, or as oxides of the metal ions,
Additionally, derivatized complexes of the metal ions may be bound to lipid head groups,. . .

CLMEN. . . peptides selected from the group consisting of melanin concentrating hormone, melanin stimulating hormone, trypsin inhibitor, Bowman Burk inhibitor, luteinizing hormone releasing hormone, bombesin, cholecystokinin, insulin, gastrin, endorphins, enkephalins, growth hormone, prolactin, oxytocin, follicle stimulating hormone, human chorionic gonadotropin, corticotropin, 0-lipotropin, 7-lipotropin,

calcitonin, glucagon, thyrotropin, elastin, cyclosporin, and collagen, and. . .

. . .

peptides selected from the group consisting of melanin concentrating hormone, melanin stimulating hormone, trypsin inhibitor, Bowman Burk inhibitor, luteinizing hormone releasing hormone, bombesin, cholecystokinin, insulin, 10 gastrin,, endorphins, enkephalins, growth hormone, prolactin, oxytocin, follicle stimulating hormone, human chorionic gonadotropin, corticotropin, fl-lipotropin, T-lipotropin, calcitonin, glucagon, thyrotropin, elastin, cyclosporin, and collagen,. . .

L27 ANSWER 5 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995005842 PCTFULL ED 20020514
TITLE (ENGLISH): METHOD AND DEVICE FOR TREATING GASTROINTESTINAL MUSCLE DISORDERS AND OTHER SMOOTH MUSCLE DYSFUNCTION
TITLE (FRENCH): PROCEDE ET DISPOSITIF POUR TRAITER LES TROUBLES MUSCULAIRES GASTRO-INTESTINAUX ET AUTRES DYSFONCTIONNEMENTS DES MUSCLES LISSES
INVENTOR(S): PASRICHA, Pankaj, J.;
KALLOO, Anthony, N.
PATENT ASSIGNEE(S): THE JOHNS HOPKINS UNIVERSITY
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9505842	A1	19950302

DESIGNATED STATES
W: CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1994-US9759 A 19940823
PRIORITY INFO.: US 1993-112,088 19930826

DETD Figs. 3A and B show the effect of intrasphincteric injection of BoTx on LES response to cholecystokinin octapeptide (CCK)

. . .

0.01). The response of the LES to the IV administration of edrophonium (Tensilon; ICN Pharmaceuticals Inc., Costa Mesa, CA) and cholecystokinin
octapeptide (CCK-8) (Kinevac; ER Squibb amp;Sons, Princeton, NJ) in three
additional piglets was also measured. LES pressures, measured by a DENTSLEEVE, were. . .

. . .

retention studies
After an overnight fast, patients were asked to ingest a corn-flake meal with milk containing 0.531 mci 99 aiTc DTPA. Subsequently, serial dynamic
images were obtained with the subject sitting erect in front of a gamma camera.
Retention was expressed. . .

L27 ANSWER 6 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1994004674 PCTFULL ED 20020513
TITLE (ENGLISH): HUMAN MELANOCYTE STIMULATING HORMONE RECEPTOR
TITLE (FRENCH): RECEPTEUR D'HORMONE STIMULANT LE MELANOCYTE CHEZ L'HOMME
INVENTOR(S): WIKBERG, Jarl;
CHHAJLANI, Vijay
PATENT ASSIGNEE(S): WIKBERG, Jarl;
CHHAJLANI, Vijay
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE

	WO 9404674	A1	19940303

DESIGNATED STATES
W: AU BB BG BR BY CA CZ FI HU JP KP KR KZ LK MG MN MW NO NZ PL RO RU SD SK UA US VN AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1993-DK273	A	19930820
PRIORITY INFO.:	DK 1992-1046/92		19920821
	DK 1992-1118/92		19920910
	DK 1993-528/93		19930505

DETD . . . the substance P receptor, substance K receptor, endothelin receptor, angiotensin receptor, chemoattractant peptide receptor, bombesin receptor, oxytocin receptor, vasopressin receptor, antidiuretic hormone receptor, gastrin receptor, cholecystokinin receptor, canabinoid receptor, follicle stimulating hormone receptor, luteinizing hormone receptor, growth hormone receptor, thyrotropin receptor,, calcitonin receptor, calcitonin gene related peptide receptor and/or parathyroid. . .

isothiocyanatobenzyl EDTA (CITC), diethylenetriaminepenta-acetic acid (DTPA) and be coupled via the mixed anhydride or the cyclic anhydride (Hnatowich 1990). However, since such complexes may provide somewhat unstable chelation and more-over during their manufacture intra and intermolecular cross linking of antibodies, other chelators such as e.g. GYK-DTPA or SCN-Bz-DTPA may be used as an alternative (Hnatowich 1990). Radiolabelling of 99mTc to the antibody may be afforded by using direct labelling techniques. . .

L27 ANSWER 7 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN

ACCESSION NUMBER:	1993018797 PCTFULL ED 20020513
TITLE (ENGLISH):	METHOD OF INTRAOPERATIVELY DETECTING AND LOCATING TUMORAL TISSUES
TITLE (FRENCH):	PROCEDE POUR DETECTER ET LOCALISER DE FACON PEROPERATOIRE DES TISSUS TUMORAUX
INVENTOR(S):	ENSING, Geert, Jacob; PANEK, Karel, Jan; DOEDENS, Bareld, Jan
PATENT ASSIGNEE(S):	MALLINCKRODT MEDICAL, INC.; ENSING, Geert, Jacob; PANEK, Karel, Jan; DOEDENS, Bareld, Jan
LANGUAGE OF PUBL.:	English
DOCUMENT TYPE:	Patent

PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9318797	A1	19930930

DESIGNATED STATES
W: AU CA JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

APPLICATION INFO.:	WO 1993-US2772	A	19930324
PRIORITY INFO.:	NL 1992-92200848.7		19920325

DETD . . . thyroid-stimulating hormone, vasoactive intestinal polypeptide, prolactin, thyrotropin-releasing hormone, insulin, adrenocorticotropic hormone (ACTH), in particular o(--MSH (melanocyte-stimulating hormone) and f -(methylsulfonyl)-L- c4-aminobutyryl-L-d-glutamyl-L-histidyl-L-

0 phenylaianyl-D-lysyl-L-phenylaianine, cholecystokinin, corticotropin-releasing
hormone (CRH), growth hormone-releasing hormone (GRH), arginine and lysine
vasopressin, oxytocin, glucagon, secretin, parathyroid hormone (PTH) and PTH
related peptide.

bond to an amino group of said
peptide and is derived from ethylene diamine tetra-acetic acid (EDTA), di-
ethylene triamine penta-acetic acid (DTPA), ethyleneglycol-0,0'-bis(2-
aminoethyl)-N,N,N',N'-tetra-acetic acid (EGTA), N,N-bis(hydroxybenzyl)-
ethylenediamine-N,N'-diacetic acid (HBED), triethylene tetramine hexa-acetic
acid (TTHA), 1,4,7,10-tetraazacyclododecane-N,N',N,N'-tetra-acetic acid
(DOTA), 1 8,11-tetra-azacyclotetradecane-NN',N,N'-tetra-acetic acid
(TETA),, 1 diaminocyclohexane tetra-acetic acid (DCTA), substituted DTPA,
substituted EDTA, or from a compound of the general formula
-R-
S] Y
wherein R is a branched or non-branched, optionally substituted hydrocarbyl
radical,.

A, Preparation of DTPA-Octreotide kit
The DTPA-Octreotide kit formulated on basis of sodium acetate buffer with the final composition
3,89 mg sodium acetate
0,029 mg acetic acid
10 gg DTPA-Octreotide
per vial is prepared as follows.

To formulate the kit, 0,5 mg of DTPA-Octreotide is dissolved in 4 ml of acetic acid solution, and 5 ml of sodium acetate solution are added.

In a similar way, starting from 2.5 mg DTPA-Octreotide was also prepared and a kit containing 50gg DTPA-Octreotide per vial.

C, Labelling of DTPA-Octreotide kit with Tb
Several kits of DTPA-Octreotide, prepared according to Example I containing 10 or 50 gg DTPA-Octreotide, are labelled by addition of 0.5 ml of Tb-161 solution obtained under B. The mixture is incubated for 30 min. at room temperature.

ITLC as described above,
Tb DTPA-Octreotide Rf ca 0 0.6
Free Tb-161 Rf ca 0,9 0
Hydrolysed Tb-161 Rf ca 0 0,1
HPLC: Column: gBondapakBC 18 10pn, 3.9 x.

>92%
78.4% >93%
challenge experiment with serum (bovine), added at 24 h
76.4% >95%
Free Tb-161 was not detectable in any kit containing 50 gg DTPA-Octreotide.

h - HPLC 96.2%

HPLC identification positive, because UV spectrum and activity peaks of Tb-161 are found identical with those for In-III labelled DTPA-Octreotide used as control.

EXAMPLE 11
Labelling of DTPA-Octreotide kit with Yb-175 and its use in combination with detectincr agent DTPA I-Tvr'-Octreotide
A. Labellincf of DTPA-Octreotide kit with Yb
Ca 1 mg of enriched (97.8%) 174-Yb2O2 is irradiated for 48 hours in a nuclear reactor with thermal. . .

Several kits containing 10 gg of DTPA-Octreotide prepared according to Example I are labelled by addition of I ml of the Yb-175 stock solution. The mixture is let to-incubate 30. . .

Yb-175 Octreotide: LY at 3 ho ITLC Rf 0 06 91,2%
at 24 h. ITLC Rf 0,5-06 91,7%
B, Preiparation of DTPA 125-Tyr3-Octreotide.

DTPA-Tyr3-Octreotide of the formula
DTPA- (D) Phe-Cys -Tyr*- (D) Trp-Lys -Thr-Cys -Throl
is prepared from Tyr3-Octreotide in a corresponding manner as described in Int, Pat, Appln, WO. . . Example 1, and further iodinated with 125I sodium iodide, dissolved in phosphate buffer in the presence of chloramine T. The molar ratio of DTPA-Tyr3-Octreotide; chloramine T: 125-I is 1:4,6:0,6 The reaction is terminated with 10% BSA solution. The labelled product of the above formula wherein Tyr] =. . .

To combine the therapeutical effect with the radioguided surgery are used both preparations; Yb Octreotide for the desired therapeutic effect and DTPA I-Tyr 3_ Octreotide as the detectingu agent,
Depending on the conditions, they can be used separately, in this case by administering Yb Octreotide first to cause partial or deep tumour necrosis, followed by administration of DTPA I-Tyr3-Octreotide to guide the tumours removal, or they can be administered simultaneously as a mixture in an appropriate ratio. Such a mixture. . .

EXAMPLE III
Labelling of DTPA-Octreotide kit with Ho-166 and its use in combination with Octreotide labelled with Tb
A. Labelling of DTPA-Octreotide kit with Ho 6-
Ca 1 mg of natural (monoisotopic) 165-Ho2O3 is irradiated for 48 hours in nuclear reactor with a thermal. . .

Several kits, containing lOgg of DTPA-Octreotide prepared according to Example I., are labelled by addition of 0.5 or 1 ml of Ho-166 stock solution. The mixture is let. . .

Labelled Ho Octreotide 9111%
Free Ho-166 8,9%
B. Pre-oaration of DTPA-Tb Octreotide as described in Example I., with kit containing 50 Ltq DTPA-Octreotide.

CLMEN. . . amide bond to an amino group of said peptide and being derived from ethylene diamine tetra-acetic acid (EDTA), diethylene triamine penta-acetic acid (DTPA), ethyleneglycol-0,01-bis(2-aminoethyl)-N,N,N',N'-tetra-acetic acid (EGTA), N,N.bis(hydroxybenzyl)-

ethylenediamine-N,N'-diacetic acid (HBED), triethylene tetramine hexa-acetic
acid (TTHA), 1,4,7,10-tetraazacyclododecane-N,N,N,Nf-tetra-acetic acid (DOTA),, 1 8,,11-tetra-azacyclotetradecane-N,N',N,N'-tetra-acetic acid
(TETA), 1,2-diaminocyclohexane tetra-acetic acid (DCTA), substituted DTPA,
substituted EDTA, or from a
compound of the general formula
NO
wherein R is a branched or non-branched, optionally substituted hydrocarbyl
radical, which may be. . .

L27 ANSWER 8 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1992004916 PCTFULL ED 20020513
TITLE (ENGLISH): PARTICULATE AGENTS
TITLE (FRENCH): AGENTS SOUS FORME DE PARTICULES
INVENTOR(S): FILLER, Aaron, Gershon
PATENT ASSIGNEE(S): ST. GEORGE'S ENTERPRISES LIMITED;
FILLER, Aaron, Gershon
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

	NUMBER	KIND	DATE
	WO 9204916	A2	19920402

DESIGNATED STATES
W: AT AU BE CA CH DE DK ES FR GB GR IT JP LU NL NO SE US
APPLICATION INFO.: WO 1991-EP1780 A 19910913
PRIORITY INFO.: GB 1990-9020075.9 19900914
GB 1990-9023580.5 19901030
GB 1990-9027293.1 19901217
GB 1991-9100233.7 19910107
GB 1991-9100981.1 19910116
GB 1991-9102146.9 19910131
GB 1991-9110876.1 19910520
GB 1991-9116373.3 19910730
GB 1991-9117851.7 19910819
GB 1991-9118676.7 19910830

DETD Paramagnetic contrast agents such as gadolinium-DTPA act primarily by altering T, relaxation rates.
. . .
its ease of use as a
histocheiAcal marker. Other studies have demonstrated transport of a wide variety of substances including Vasoactive Intestinal Polypeptide (VIP),
cholecystokinin, substance P and somatostatin, neuropeptide-Y, and adriamycin. These types of tracers have sometimes been introduced by intravenous injection with subsequent uptake by neurons. . .

The use of a magnetic resonance small molecule contrast agent such as gadolinium-DTPA (diethylene-triaminepentaacetic acid) required the introduction of a very high concentration into the nerve and this amount was beyond what could be achieved,. . .

6) A wide variety of peptides and small proteins such as endorphins, vasoactive intestinal polypeptide, calcitonin gene-related peptide, cholecystokinin, substance P, somatostatin, and neuropeptide Y or the relevant portions of such peptides for the encouragement

of neuronal uptake and transport.

Additional types of agents for imaging include paramagnetic metal chelates of polychelants (e.g. poly-lysine gadolinium-DTPA 40 which uses the macromolecularlparticulate aspects of uptake to introduce groups of paramagnetic nuclei (40 Gd atoms per molecule) (see EP-A-305320, EP-A-357622, EP-A-355097, EP-A-331616,. . .

L27 ANSWER 9 OF 10 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1992001469 PCTFULL ED 20020513
TITLE (ENGLISH): A COMPOSITION PROVIDING IMPROVED CLEARANCE OF BIOACTIVE SUBSTANCES FROM THE BLOODSTREAM
TITLE (FRENCH): COMPOSITION ASSURANT UNE MEILLEURE ELIMINATION DE SUBSTANCES BIOACTIVES CONTENUES DANS LE SYSTEME SANGUIN
INVENTOR(S): SELMER, Johan
PATENT ASSIGNEE(S): NOVO NORDISK A/S;
SELMER, Johan
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9201469	A1	19920206

DESIGNATED STATES
W: AT AU BE CA CH CS DE DK ES FI FR GB GR HU IT JP KR LU NL NO PL SE SU US
APPLICATION INFO.: WO 1991-DK215 A 19910724
PRIORITY INFO.: DK 1990-1762/90 19900724

DETD . . . radioimaging leukocytes by injecting a conjugate of an antibody reactive with a leukocyt6 surface molecule and a radioisotope chelated with an EDTA or DTPA derivative followed by the injection of an antibody against the conjugate in order to clear the conjugate/antibody complex through the reticuloendothelial system.. . .
. . .
hormone,,;
follicle-Stimulating
hormone,, luteinising
h o r m o n e r
adrenocorticotropic
hormone, parathyroidea
hormone, prolactin,
l i p o t r o p i n J,
cholecystokinin,
calcitonin, secretin,
atrialnatriuretic
factor, endothelin,
vasoactive intestinal
p o l y p e p t i d e r
transferrin, tachykinin
Intercellular adhesion
factors intercellular adhesion
molecule 1, endothelial
leukocyte. . .

=> octapeptide
OCTAPEPTIDE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

```
=> s octapeptide
          1500 OCTAPEPTIDE
           238 OCTAPEPTIDES
L28       1631 OCTAPEPTIDE
                (OCTAPEPTIDE OR OCTAPEPTIDES)

=> s l28 and (DTPA or DOTA)
          5576 DTPA
            12 DTPAS
          5579 DTPA
                (DTPA OR DTPAS)
          1767 DOTA
             5 DOTAS
          1768 DOTA
                (DOTA OR DOTAS)
L29         86 L28 AND (DTPA OR DOTA)

=> s l29 not py>1996
        935225 PY>1996
L30         15 L29 NOT PY>1996

=> s l30 and CCK
          2003 CCK
            36 CCKS
          2007 CCK
                (CCK OR CCKS)
L31          1 L30 AND CCK

=> d ibib

L31    ANSWER 1 OF 1      PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        1995005842 PCTFULL  ED 20020514
TITLE (ENGLISH):         METHOD AND DEVICE FOR TREATING GASTROINTESTINAL MUSCLE
                         DISORDERS AND OTHER SMOOTH MUSCLE DYSFUNCTION
TITLE (FRENCH):          PROCEDE ET DISPOSITIF POUR TRAITER LES TROUBLES
                         MUSCULAIRES GASTRO-INTESTINAUX ET AUTRES
                         DYSFONCTIONNEMENTS DES MUSCLES LISSES
INVENTOR(S):             PASRICHA, Pankaj, J.;
                         KALLOO, Anthony, N.
PATENT ASSIGNEE(S):      THE JOHNS HOPKINS UNIVERSITY
DOCUMENT TYPE:           Patent
PATENT INFORMATION:
                         NUMBER              KIND     DATE
                         ---------------------------------
                         WO 9505842          A1 19950302
DESIGNATED STATES
      W:                 CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.:       WO 1994-US9759       A  19940823
PRIORITY INFO.:          US 1993-112,088         19930826


=> d kwic

L31    ANSWER 1 OF 1      PCTFULL   COPYRIGHT 2006 Univentio on STN

DETD   Figs. 3A and B show the effect of intrasphincteric injection of BoTx on
       LES response to cholecystokinin octapeptide (CCK)
       .
       The response of the LES to the IV administration of edrophonium
       (Tensilon; ICN Pharmaceuticals Inc., Costa Mesa, CA) and cholecystokinin
         octapeptide (CCK-8) (Kinevac; ER Squibb amp;Sons,
       Princeton, NJ) in three
       additional piglets was also measured. LES pressures, measured by a
       DENTSLEEVE, were recorded in response to IV edrophonium (5 mg). After a
       SUBSTITUTE SHEET (RULE 26)
```

washout period of 10 minutes, CCK (5 µg IV) was then administered.
Subsequently, BoTx was injected into the LES, as described above, and the
experiment was. . .

Intrasphincteric BoTx also altered the response of the LES to CCK
(Figure 3). In untreated piglets, CCK did not cause any significant change in
LES pressure. However, after intrasphincteric BoTx injection, a significant
increase in LES pressure was seen in response to CCK. It should be noted that
despite what was felt to be an adequate washout period (10 minutes) in between
injections, basal. . . .

retention studies
After an overnight fast, patients were asked to ingest a corn-flake meal with milk containing 0.531 mci 99 aiTc DTPA. Subsequently, serial dynamic
images were obtained with the subject sitting erect in front of a gamma camera.
Retention was expressed. . .

=> d his

(FILE 'HOME' ENTERED AT 13:35:48 ON 07 DEC 2006)

FILE 'REGISTRY' ENTERED AT 13:36:14 ON 07 DEC 2006
L1 136 S DY'NLE'GW'NLE'DF/SQSP
L2 424 S DYMGWMDF/SQSP

FILE 'CAPLUS' ENTERED AT 13:39:00 ON 07 DEC 2006
L3 84 S L1
L4 0 S DPTA AND L3
L5 5 S DOTA AND L3
L6 134722 S CHELAT?
L7 12 S L6 AND L3
L8 0 S L7 NOT PY>1997
L9 1 S L7 NOT PY>1998
L10 4485 S L2
L11 49 S L10 AND L6
L12 20 S L11 NOT PY>1997
L13 20 S L11 NOT PY>1996
L14 14458 S METAL CHELAT?
L15 3 S L14 AND L10
L16 4 S L10 AND (DPTA OR DOTA)
L17 9 S L10 AND DTPA

FILE 'DISSABS' ENTERED AT 13:46:43 ON 07 DEC 2006
L18 323 S CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK () 8))
L19 360 S DTPA OR DOTA
L20 2 S L19 AND L18
L21 497 S METAL CHELAT?
L22 0 S L21 AND L18

FILE 'PCTFULL' ENTERED AT 13:50:53 ON 07 DEC 2006
L23 2006 S CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK () 8))
L24 2224 S DPTA OR DOTA
L25 6121 S DTPA OR DOTA
L26 110 S L25 AND L23
L27 10 S L26 NOT PY>1996

```
L28         1631 S OCTAPEPTIDE
L29           86 S L28 AND (DTPA OR DOTA)
L30           15 S L29 NOT PY>1996
L31            1 S L30 AND CCK

=> s l23 and chelat?
         44321 CHELAT?
L32        591 L23 AND CHELAT?

=> s l32 and (radio? or imag?)
        190519 RADIO?
        202203 IMAG?
L33        495 L32 AND (RADIO? OR IMAG?)

=> s l33 not py>1996
        935225 PY>1996
L34         34 L33 NOT PY>1996

=> d his

     (FILE 'HOME' ENTERED AT 13:35:48 ON 07 DEC 2006)

     FILE 'REGISTRY' ENTERED AT 13:36:14 ON 07 DEC 2006
L1          136 S DY'NLE'GW'NLE'DF/SQSP
L2          424 S DYMGWMDF/SQSP

     FILE 'CAPLUS' ENTERED AT 13:39:00 ON 07 DEC 2006
L3           84 S L1
L4            0 S DPTA AND L3
L5            5 S DOTA AND L3
L6       134722 S CHELAT?
L7           12 S L6 AND L3
L8            0 S L7 NOT PY>1997
L9            1 S L7 NOT PY>1998
L10        4485 S L2
L11          49 S L10 AND L6
L12          20 S L11 NOT PY>1997
L13          20 S L11 NOT PY>1996
L14       14458 S METAL CHELAT?
L15           3 S L14 AND L10
L16           4 S L10 AND (DPTA OR DOTA)
L17           9 S L10 AND DTPA

     FILE 'DISSABS' ENTERED AT 13:46:43 ON 07 DEC 2006
L18         323 S CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK () 8))
L19         360 S DTPA OR DOTA
L20           2 S L19 AND L18
L21         497 S METAL CHELAT?
L22           0 S L21 AND L18

     FILE 'PCTFULL' ENTERED AT 13:50:53 ON 07 DEC 2006
L23        2006 S CHOLECYSTOKININ OR (CCK-8 OR CCK8 OR (CCK () 8))
L24        2224 S DPTA OR DOTA
L25        6121 S DTPA OR DOTA
L26         110 S L25 AND L23
L27          10 S L26 NOT PY>1996
L28        1631 S OCTAPEPTIDE
L29          86 S L28 AND (DTPA OR DOTA)
L30          15 S L29 NOT PY>1996
L31           1 S L30 AND CCK
L32         591 S L23 AND CHELAT?
L33         495 S L32 AND (RADIO? OR IMAG?)
L34          34 S L33 NOT PY>1996

=> s l34 and l28
```

L35 8 L34 AND L28

=> d ibib 1-8

L35 ANSWER 1 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1996039161 PCTFULL ED 20020514
TITLE (ENGLISH): MULTI-TYROSINATED SOMATOSTATIN ANALOGS
TITLE (FRENCH): ANALOGUES DE LA SOMATOSTATINE CONTENANT PLUSIEURS DE TYROSINES
INVENTOR(S): COY, David, H.;
WOLTERING, Eugene, A.;
O'DORISIO, M., Sue;
O'DORISIO, Thomas, M.;
MURPHY, William, A.
PATENT ASSIGNEE(S): THE ADMINISTRATORS OF THE TULANE EDUCATIONAL FUND ;
THE OHIO STATE UNIVERSITY RESEARCH FOUNDATION;
THE LOUISIANA STATE UNIVERSITY MEDICAL CENTER FOUNDATION;
CHILDREN'S HOSPITAL, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9639161	A1	19961212

DESIGNATED STATES
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.: WO 1996-US8437 A 19960603
PRIORITY INFO.: US 1995-8/462,223 19950605

L35 ANSWER 2 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1994023724 PCTFULL ED 20020513
TITLE (ENGLISH): MEMBRANE-PERMEANT SECOND MESSENGERS
TITLE (FRENCH): MESSAGERS SECONDAIRES S'INFILTRANT DANS LA MEMBRANE CELLULAIRE
INVENTOR(S): TSIEN, Roger, Y.;
SCHULTZ, Carsten
PATENT ASSIGNEE(S): THE REGENTS OF THE UNIVERSITY OF CALIFORNIA
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9423724	A1	19941027

DESIGNATED STATES
W: AU BB BG BR BY CA CN CZ FI HU JP KP KR KZ LK LV MG MN MW NO NZ PL RO RU SD SI SK UA UZ VN AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.: WO 1994-US3889 A 19940408
PRIORITY INFO.: US 1993-45,585 19930409

L35 ANSWER 3 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1994022444 PCTFULL ED 20020513
TITLE (ENGLISH): TRICYCLIC COMPOUNDS FOR INHIBITING PLATELET AGGREGATION
TITLE (FRENCH): COMPOSES TRICYCLIQUES UTILISES POUR INHIBER L'AGREGATION PLAQUETTAIRE
INVENTOR(S): CALLAHAN, James, Francis;
HUFFMAN, William, F.
PATENT ASSIGNEE(S): SMITHKLINE BEECHAM CORPORATION;

CALLAHAN, James, Francis;
HUFFMAN, William, F.

LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9422444	A1	19941013

DESIGNATED STATES
W: JP US AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1994-US3383 A 19940329
PRIORITY INFO.: US 1993-8/038,382 19930329

L35 ANSWER 4 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1993008842 PCTFULL ED 20020513
TITLE (ENGLISH): HEMOGLOBINS AS DRUG DELIVERY AGENTS
TITLE (FRENCH): HEMOGLOBINES UTILISEES COMME AGENTS ADMINISTRATEURS DE MEDICAMENTS
INVENTOR(S): ANDERSON, David, C.;
MATHEWS, Antony, James
PATENT ASSIGNEE(S): SOMATOGEN, INC.;
ANDERSON, David, C.;
MATHEWS, Antony, James
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9308842	A1	19930513

DESIGNATED STATES
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK LU MG MN MW NL NO PL RO RU SD SE UA US AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE BF BJ CF CG CI CM GA GN ML MR SN TD TG
APPLICATION INFO.: WO 1992-US9713 A 19921106
PRIORITY INFO.: US 1991-789,177 19911108
US 1991-789,179 19911108

L35 ANSWER 5 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1993000095 PCTFULL ED 20020513
TITLE (ENGLISH): BICYCLIC FIBRINOGEN ANTAGONISTS
TITLE (FRENCH): ANTAGONISTES BICYCLIQUES DE FIBRINOGENE
INVENTOR(S): BONDINELL, William, Edward;
CALLAHAN, James, Francis;
HUFFMAN, William, Francis;
KEENAN, Richard, McCulloch;
KU, Thomas, Wen-Fu;
NEWLANDER, Kenneth, Allen
PATENT ASSIGNEE(S): SMITHKLINE BEECHAM CORPORATION;
BONDINELL, William, Edward;
CALLAHAN, James, Francis;
HUFFMAN, William, Francis;
KEENAN, Richard, McCulloch;
KU, Thomas, Wen-Fu;
NEWLANDER, Kenneth, Allen
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9300095	A2	19930107

DESIGNATED STATES
W: AU CA JP KR US AT BE CH DE DK ES FR GB GR IT LU MC NL SE
APPLICATION INFO.: WO 1992-US5463 A 19920626

PRIORITY INFO.: US 1991-723,009 19910628

L35 ANSWER 6 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1991019733 PCTFULL ED 20020513
TITLE (ENGLISH): DERIVATIVES OF TETRAPEPTIDES AS CCK AGONISTS
TITLE (FRENCH): DERIVES DE TETRAPEPTIDES EN TANT QU'AGONISTES DE CHOLECYSTOKININE
INVENTOR(S): SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kona;
HOLLADAY, Mark, W.;
LIN, Chun, W.;
NELLANS, Hugh, N.
PATENT ASSIGNEE(S): ABBOTT LABORATORIES
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9119733	A1	19911226

DESIGNATED STATES
W: AT BE CA CH DE DK ES FR GB GR IT JP LU NL SE
APPLICATION INFO.: WO 1991-US4458 A 19910620
PRIORITY INFO.: US 1990-541,230 19900620
US 1991-713,010 19910614

L35 ANSWER 7 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1990006937 PCTFULL ED 20020513
TITLE (ENGLISH): DERIVATIVES OF TETRAPEPTIDES AS CCK AGONISTS
TITLE (FRENCH): DERIVES DE TETRAPEPTIDES UTILISES COMME AGENTS REPRODUISANT L'ACTIVITE DE LA CCK
INVENTOR(S): SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kong
PATENT ASSIGNEE(S): ABBOTT LABORATORIES;
SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kong
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9006937	A1	19900628

DESIGNATED STATES
W: BE CH DE ES FR GB IT JP NL SE US
APPLICATION INFO.: WO 1989-US5673 A 19891218
PRIORITY INFO.: US 1988-287,955 19881221

L35 ANSWER 8 OF 8 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1990006128 PCTFULL ED 20020513
TITLE (ENGLISH): METHODS AND COMPOSITIONS FOR INHIBITING PLATELET AGGREGATION
TITLE (FRENCH): METHODES ET COMPOSITIONS POUR INHIBER L'AGREGATION DES PLAQUETTES
INVENTOR(S): MARAGANORE, John, M.;
JAKUBOWSKI, Joseph, A.
PATENT ASSIGNEE(S): BIOGEN, INC.;
TRUSTEES OF BOSTON UNIVERSITY
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

```
                        NUMBER              KIND     DATE
                        ---------------------------------
                        WO 9006128          A1 19900614
DESIGNATED STATES
      W:                DK FI HU JP KR NO
APPLICATION INFO.:      WO 1989-US849       A  19890302
PRIORITY INFO.:         US 1988-280,618        19881205


=> s l35 and cck
          2003 CCK
            36 CCKS
          2007 CCK
                 (CCK OR CCKS)
L36           5 L35 AND CCK

=> d ibib 1-5

L36    ANSWER 1 OF 5     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:       1996039161 PCTFULL  ED 20020514
TITLE (ENGLISH):        MULTI-TYROSINATED SOMATOSTATIN ANALOGS
TITLE (FRENCH):         ANALOGUES DE LA SOMATOSTATINE CONTENANT PLUSIEURS DE
                        TYROSINES
INVENTOR(S):            COY, David, H.;
                        WOLTERING, Eugene, A.;
                        O'DORISIO, M., Sue;
                        O'DORISIO, Thomas, M.;
                        MURPHY, William, A.
PATENT ASSIGNEE(S):     THE ADMINISTRATORS OF THE TULANE EDUCATIONAL FUND ;
                        THE OHIO STATE UNIVERSITY RESEARCH FOUNDATION;
                        THE LOUISIANA STATE UNIVERSITY MEDICAL CENTER
                        FOUNDATION;
                        CHILDREN'S HOSPITAL, INC.
LANGUAGE OF PUBL.:      English
DOCUMENT TYPE:          Patent
PATENT INFORMATION:
                        NUMBER              KIND     DATE
                        ---------------------------------
                        WO 9639161          A1 19961212
DESIGNATED STATES
      W:                AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI
                        GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD
                        MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM
                        TR TT UA UG UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD
                        RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL
                        PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.:      WO 1996-US8437      A  19960603
PRIORITY INFO.:         US 1995-8/462,223      19950605

L36    ANSWER 2 OF 5     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:       1994023724 PCTFULL  ED 20020513
TITLE (ENGLISH):        MEMBRANE-PERMEANT SECOND MESSENGERS
TITLE (FRENCH):         MESSAGERS SECONDAIRES S'INFILTRANT DANS LA MEMBRANE
                        CELLULAIRE
INVENTOR(S):            TSIEN, Roger, Y.;
                        SCHULTZ, Carsten
PATENT ASSIGNEE(S):     THE REGENTS OF THE UNIVERSITY OF CALIFORNIA
LANGUAGE OF PUBL.:      English
DOCUMENT TYPE:          Patent
PATENT INFORMATION:
                        NUMBER              KIND     DATE
                        ---------------------------------
                        WO 9423724          A1 19941027
DESIGNATED STATES
      W:                AU BB BG BR BY CA CN CZ FI HU JP KP KR KZ LK LV MG MN
```

MW NO NZ PL RO RU SD SI SK UA UZ VN AT BE CH DE DK ES
FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN
ML MR NE SN TD TG

APPLICATION INFO.: WO 1994-US3889 A 19940408
PRIORITY INFO.: US 1993-45,585 19930409

L36 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1993008842 PCTFULL ED 20020513
TITLE (ENGLISH): HEMOGLOBINS AS DRUG DELIVERY AGENTS
TITLE (FRENCH): HEMOGLOBINES UTILISEES COMME AGENTS ADMINISTRATEURS DE MEDICAMENTS
INVENTOR(S): ANDERSON, David, C.;
MATHEWS, Antony, James
PATENT ASSIGNEE(S): SOMATOGEN, INC.;
ANDERSON, David, C.;
MATHEWS, Antony, James
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9308842	A1	19930513

DESIGNATED STATES
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK
LU MG MN MW NL NO PL RO RU SD SE UA US AT BE CH DE DK
ES FR GB GR IE IT LU MC NL SE BF BJ CF CG CI CM GA GN
ML MR SN TD TG

APPLICATION INFO.: WO 1992-US9713 A 19921106
PRIORITY INFO.: US 1991-789,177 19911108
US 1991-789,179 19911108

L36 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1991019733 PCTFULL ED 20020513
TITLE (ENGLISH): DERIVATIVES OF TETRAPEPTIDES AS CCK AGONISTS
TITLE (FRENCH): DERIVES DE TETRAPEPTIDES EN TANT QU'AGONISTES DE CHOLECYSTOKININE
INVENTOR(S): SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kona;
HOLLADAY, Mark, W.;
LIN, Chun, W.;
NELLANS, Hugh, N.
PATENT ASSIGNEE(S): ABBOTT LABORATORIES
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9119733	A1	19911226

DESIGNATED STATES
W: AT BE CA CH DE DK ES FR GB GR IT JP LU NL SE
APPLICATION INFO.: WO 1991-US4458 A 19910620
PRIORITY INFO.: US 1990-541,230 19900620
US 1991-713,010 19910614

L36 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1990006937 PCTFULL ED 20020513
TITLE (ENGLISH): DERIVATIVES OF TETRAPEPTIDES AS CCK AGONISTS
TITLE (FRENCH): DERIVES DE TETRAPEPTIDES UTILISES COMME AGENTS REPRODUISANT L'ACTIVITE DE LA CCK
INVENTOR(S): SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kong

PATENT ASSIGNEE(S): ABBOTT LABORATORIES;
SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kong
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9006937	A1	19900628

DESIGNATED STATES
W: BE CH DE ES FR GB IT JP NL SE US
APPLICATION INFO.: WO 1989-US5673 A 19891218
PRIORITY INFO.: US 1988-287,955 19881221

=> d ibib kwic 5

L36 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1990006937 PCTFULL ED 20020513
TITLE (ENGLISH): DERIVATIVES OF TETRAPEPTIDES AS CCK AGONISTS
TITLE (FRENCH): DERIVES DE TETRAPEPTIDES UTILISES COMME AGENTS REPRODUISANT L'ACTIVITE DE LA CCK
INVENTOR(S): SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kong
PATENT ASSIGNEE(S): ABBOTT LABORATORIES;
SHIOSAKI, Kazumi;
NADZAN, Alex, M.;
KOPECKA, Hana;
SHUE, Youe-Kong
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9006937	A1	19900628

DESIGNATED STATES
W: BE CH DE ES FR GB IT JP NL SE US
APPLICATION INFO.: WO 1989-US5673 A 19891218
PRIORITY INFO.: US 1988-287,955 19881221
TIEN DERIVATIVES OF TETRAPEPTIDES AS CCK AGONISTS
TIFR DERIVES DE TETRAPEPTIDES UTILISES COMME AGENTS REPRODUISANT L'ACTIVITE DE LA CCK
ABEN Tetrapeptide analogs are disclosed which possess CCK agonist activity.
ABFR Les analogues de tetrapeptides decrits possedent une activite similaire a la cholecystokinine (CCK).

DETD DERTVATIVES OF-TETRAPEPTIDES AS CCK AGONISTS
This is a continuation-in-part of U.S. Patent Application Serial No. 287,955, filed December 21, 1988.

Technical Field
The present invention relates to novel organic compounds and compositions which mimic the effects of cholecystokinin, caerulein and gastrin, processes for making such compounds, synthetic intermediates employed in these processes and a method for treating gastrointestinal disorders, central nervous. . .

Backaround of thp Tnvention

Cholecystokinin (CCK) is a 39 amino acid polypeptide hormone. CCK and a 33 amino acid fragment of CCK (CCK 33) were first isolated from hog intestine (Mutt and jorpes, Biochem.]L, 12,Ij 628 (1981)). Recently the CCK 33 fragment has been found in the brain, where it appears to be the precursor of two smaller fragments, an octapeptide CC]K8 and a tetrapeptide CCK 4 (Dockray, Nature 264 402 (1979)).

Existence of these fragments in the cortex of the brain suggests that CCK may be an important neuromodulator of memory, learning and control of the primary sensory and motor functions. CCK and it-s fragments are believed to play an important role in appetite regulation and satiety (Della-Ferat Science 206 471 (1979); Saito et. . . Eating and it-s Disorders, eds., Raven Pressr New Yorkf 67 (1984)). Recently,, patients with bulimia were shown to have lower than normal CCK levels in their plasma-(Geracioti, et al., New England Journal of Medici=, 3_12 683 (1988)). An additional role for CCK in the periphery is to regulate the release of insulin., CCK has been shown to increase the levels of insulin when administered to mammals (Rushakoff, et al., J. Clin. Endocrinol, Metab. 65 395. . .

C-terminal fragments of CCK have recently been reported to function as CCK receptor antagonists (Jensen et al Biochem. Biophys. Acta, 757, 250 (1983); Spanarkel, J. Biol. Chem. ZUt 6746 (1983)). Japanese patent application 45/10506 to. . .

In contrast, the present invention relates to tetrapeptide analogs-which function as agonists of CCK activity, CCK agonists are useful in the treatment and prevention of CCK-related disorders of the gastrointestinal, appetite (obesity and bulimia, among others) and insulin regulatory systems of animals, especially man. CCK agonists are also useful as central nervous system suppressants which can exhibit anti-psychotic, neuroleptic, anxiolytic, and anti-convulsant effects, among other effects on. . .

.

the Drawinas

Figure I is a plot comparing the mean level of liquid food intake (mls) for rats after chronic administration of vehicle, CCK-8 (10 nmol/kg), or the compound of Example 180 (1 nmol/kg or 10 nm/kg).

Figure 2 is a plot comparing the mean change in body weight (grams) for rats after chronic administration of vehicle, CCK-8 (10 nmol/kg), or the compound of Example 180 (1 nmol/kg or 10 nm/kg),

Summary of the Invention

In accordance with the present invention there are cholecystokinin agonists of the formula.

.

IL 1981, p 617) wherein the Boc or Cbz protected amino acid is treated with a base in the presence of a chelating agent such as a crown ether and then quenched with methyl iodide.

.

found: C 61.11r H 6.50F. N 10.89,

The compounds of formula I are CCKagonists which are useful in the treatment and prevention of CCK-related disorders of the gastrointestinal, central nervous, and appetite and insulin regulatory systems of animals and humans. As CCK agonists, they are useful in the treatment and prevention of neuroleptic disorders, tardive dyskinesiat disorders of memory and cognition, Parkinson's disease, Huntington's chorea,. . .

The ability of the compounds of the invention to interact with CCK receptors and to act as CCK agonists can
be demonstrated ja vitro using the following protocols.

CCK8 [Asp-Tyr(SO 3H)-Met-Gly-Trp-
Met-Asp-Phe-NH2], bestatin and phosphoramidon were purchased from Peptide International (Louisville, KY), EGTAr HEPES and BSA were purchased from Sigma Chemical Co.

(St. Louis,, MO), 125 11 - Bolton-Hunter (BH-CCK (specific activity, 2200 Ci/mmol) was obtained from New England Nuclear (Boston, MA). Male guïnea pigs, 250 to 32S g, were obtained from Scientific Small Animal Laboratory and Farm (Arlington Heights, IL). Collagenase, code CLSPA was purchased from Worthington (Frehold, New Jersey)
Protocol For Radioligand Binding Experiments
in Guinea Pig Cerebral Cortical and
Pancreatic Membrane PreT)arations
Cortical and pancreatic membranes were prepared as described (Lin and Miller; J, Pharmacol,. . .

Incubation Conditions
1 125 I]Bolton-Hu-nter CCK and test compounds were
8
diluted with HEPES-EGTA-salt buffer (see above) containing 0.5% bovine serum albumin (BSA). To 1 mL Skatron polystyrene tubes were added 25 uL of test compounds, 25 uL of [125 IJBH-CCK and 200 uL of membrane suspension. The
8
final BSA concentration was 0.1%. The cortical tissues were incubated at 300C for 150 min.. . . 37'C for 150 min. Incubations were
terminated by filtration using Skatron Cell Harvester and SS32 microfiber filter mats. The specific binding of
125
I IIBH-CCK 8. defined as the difference between
binding in
the absence and presence of 1 uM CCK., was 85-90% of total binding in cortex and 90-95% in pancreas. IC 50 s were determined from the Hill analysis. The results. . .

Table 1
125 1aaQ7'Q'L125
Compound of I-BH-CCK 8 I-BH-CCK8
Example Pancreas Cortex
30 270
12 680
10 732
26 238
71 1480
26 1800
32 114
45 35 4700
4 7 50 4 000
4 9 4 1 815

The results indicate that compounds of the invention possess selective affinity for the pancreatic CCK receptors.

Amylase Assay
After the 30 min incubation time, the acini was resuspended in 100 volumes of KRH-BSA buffer, containing 3 uM phosphoramidon and 100 uM bestatin. While stirring, 400 uL of acini were added to 1.5 mL microcentrifuge tubes containing 50 uL of CCK., buffer, or test compounds. The final assay volume was 500 uL. Tubes were vortexed and placed in a 37'C waterbathf under 100%. . .

TABLE 2
Cgmipound of Example Amylase rele=r.----M.4aIIL
5
3
40
80
24
157 ill
180 0.74
The results indicate that compounds of the invention are CCK agonists.

Measurement of PlasMa Insulin in Mice Following Treatment With CCK or a CCK Aaonist
Male mice, 20-30 g. were used in all experiments. The animals were fed with laboratory lab chow and water ad libitum. CCK8 or the CCK agonist compound of this invention was injected into the tail vein. Two minutes later, the animals were sacrificed and the blood was collected. . . 10,000 x g for 2 minutes. The insulin levels were determined in the supernatant, i,e,, plasma, by RIA using kits obtained from Radioassay Systems Laboratory (Carson, CA.) or Novo Biolabs (Danbury, CT.).

Agonists On Insulin Secretion in Nice
% Increase In Insulin
Dose Secretion versus
Com-pound of Examr)le (nmole/kcr)]alinC Control
157 10 41
100 112
180 100 238
CCK8 3 65
10 85
30 90
100 70
The results indicate that compounds of the invention stimulate insulin secretion in yjy.Q.

Table 4
Suppression of Locmotor-Activity in Mice Followincr
IP Administration of CCK Acronists
Comvound of ExamPI& Minimal Effective Dose
CCK 0.001 micromol/kg
106 1.0 micromol/kg
157 0.03 micromol/kg
180 0.01 micromol/kg
Table 5
Sur)r)ression of Locgmotor Activity in Mice Following
JCV Administration of CCK Agonists
Comnound of Exam-ole Minimal Effective Dose

CCK8 3.0 nmol/mouse
106 10.0 nmol/mouse
157 30.0 nmol/mouse
180 1.0 nmol/mouse
The results of these tests indicate that compounds of the invention suppress locomotor activity. . .

. . .

food intake. Five minutes prior to their one hour free feeding (Purina Rat Chow), the animals were injected (i,p,) with either vehicle, CCK 8 or the compound of Example 106. The amount of food consumed was measured after subtraction of spillage. The results of this test are. . .

AdMinistration of CCK Agonists
Compound Dose Mean Food Intake
vehicle ... 9,40 grams
C-CK 20 ug/kg 6.56 grams
Example 106 1,0 mg/kg 3.49 grams
Example 106 3.0 mg/kg. . .

When a compound of formula I is used as an agonist of CCK or gastrin in a human subject, the total daily dose administered in single or divided doses may be in amounts, for example,. . .

CLMEN 5 A method for mimicking the effects of CCK on CCK receptors comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 1,

7 A CCK agonist composition comprising a pharmaceutical carrier and a therapeutically effective amount of a compound of Claim 1.

```
=> s CCK and (DOTA or DTPA)
          2003 CCK
            36 CCKS
          2007 CCK
                 (CCK OR CCKS)
          1767 DOTA
             5 DOTAS
          1768 DOTA
                 (DOTA OR DOTAS)
          5576 DTPA
            12 DTPAS
          5579 DTPA
                 (DTPA OR DTPAS)
L37         79 CCK AND (DOTA OR DTPA)

=> s l37 not py>1996
        935225 PY>1996
L38          5 L37 NOT PY>1996

=> d ibib kwic 1-5

L38    ANSWER 1 OF 5     PCTFULL   COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER:        1996005861 PCTFULL  ED 20020514
TITLE (ENGLISH):         COMPOSITIONS AND METHODS FOR THE TREATMENT OF BODY
                         WEIGHT DISORDERS, INCLUDING OBESITY
TITLE (FRENCH):          COMPOSITIONS ET PROCEDES DE TRAITEMENT DES TROUBLES
                         INHERENTS AU POIDS CORPOREL, DONT L'OBESITE
INVENTOR(S):             TARTAGLIA, Louis, A.
```

PATENT ASSIGNEE(S): MILLENIUM PHARMACEUTICALS, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9605861	A1	19960229

DESIGNATED STATES
W: AU CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1995-US10918 A 19950823
PRIORITY INFO.: US 1994-294,522 19940823
US 1995-470,868 19950606

DETD . . . These include but are not limited to the intracellular domain of receptors for such hormones as neuropeptide Y, galanin, interostatin, insulin, and CCK. Total genomic or cDNA sequences are fused to the DNA encoding an activation domain. This library and a plasmid encoding a hybrid of. . .
. . .
Eu, or others
of the lanthanide series. These metals can be attached to the antibody using such metal chelating groups as diethylenetriaminepentacetic acid (DTPA) or ethylenediaminetetraacetic acid (EDTA).

L38 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995024426 PCTFULL ED 20020514
TITLE (ENGLISH): A NOVEL EXPRESSION-CLONING METHOD FOR IDENTIFYING TARGET PROTEINS FOR EUKARYOTIC TYROSINE KINASES AND NOVEL TARGET PROTEINS
TITLE (FRENCH): NOUVEAU PROCEDE D'EXPRESSION-CLONAGE UTILISE POUR IDENTIFIER DES PROTEINES A CIBLES DES TIROSINE-KINASES EUKARYOTES, ET NOUVELLES PROTEINES CIBLES
INVENTOR(S): SCHLESSINGER, Joseph;
SKOLNIK, Edward, Y.;
MARGOLIS, Benjamin, L.
PATENT ASSIGNEE(S): NEW YORK UNIVERSITY
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9524426	A1	19950914

DESIGNATED STATES
W: AM AU BB BG BR BY CA CN CZ EE FI GE HU JP KE KG KR KZ LK LR LT LV MD MG MN MW MX NO NZ PL RO RU SD SG SI SK TJ TT UA UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.: WO 1995-US3385 A 19950313
PRIORITY INFO.: US 1994-208,887 19940311

DETD . . . lanthanide series. These metals can be attached to the peptide probe or anti-target protein antibody using such metal chelating groups as diethylenetriaminepentaacetic acid (DTPA) or ethylenediaminetetraacetic acid (EDTA).
. . .
know how to varv the aonrorrlate
is parameters without undue ex-oerimentation. Furthermore , general methods in this area are set- forth in Sa:L=cck et al - (sunra)
Materials of which solid phase carrier can be made include, but are not limited to, nitrocellulose,

cellulose, paner, substituted polystyrenes, acrylonitriles,. . .

L38 ANSWER 3 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995024225 PCTFULL ED 20020514
TITLE (ENGLISH): POLYCHELANTS
TITLE (FRENCH): POLYCHELATEURS
INVENTOR(S): MARGERUM, Lawrence;
CARVALHO, Joan;
GARRITY, Martha;
FELLMANN, Jere, Douglas
PATENT ASSIGNEE(S): NYCOMED SALUTAR, INC.;
COCKBAIN, Julian, Roderick, Michaelson;
MARGERUM, Lawrence;
CARVALHO, Joan;
GARRITY, Martha;
FELLMANN, Jere, Douglas
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9524225	A1	19950914

DESIGNATED STATES
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SG SI SK TJ TT UA UG US UZ VN KE MW SD SZ UG AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG
APPLICATION INFO.: WO 1995-GB464 A 19950303
PRIORITY INFO.: GB 1994-9404208.2 19940304

DETD Thus, Krejcarek et al (supra) disclosed how polyaminopolycarboxylic acid (PAPCA) chelants, specifically DTPA (diethylenetriaminepentaacetic acid) could be conjugated to a protein, such as human serum albumin (HSA), by reaction of the triethylamine salt of the PAPCA. . .

Unger et al. in Investigative Radiology 20:693 (1985) analyzed tumor enhancement for magnetic resonance imaging using an anti-CEA monoclonal antibody conjugated with Gd-DTPA. They found no tumor enhancement when 4 Gd atoms were bound per antibody molecule, and predicted that a far greater ratio of. . .

Thus Hnatowich et al, (supra) used the cyclic anhydride of the chelant DTPA to attach it to a protein.
. . .
has thus been used
to produce bifunctional polychelants in which the chelant moieties are residues of open chain PAPCAs, such as EDTA and DTPA, and in which the backbone molecule is a polyamine such as polylysine or polyethyleneimine.

Thus for example Manabe et al. in Biochemica et Biophysica Acta 883: 460-467 (1986) reported attaching up to 105 DTPA residues onto a poly-L-lysine backbone using the cyclic anhydride method and also attaching polylysine-polyDTPA polychelants onto monoclonal antibody (anti-HLA IgGj) using a 2-pyridyl disulphide linker achieving a substitution of up to about 42.5 chelants (DTPA resi]_-:-.-]s) per site-specific macromolecule. Torcrilin et al. in Hybridoma 6:229-240 (1987) also reported attaching DTPA and EDTA to

polyethyleneimine and polylysine backbones which were then attached to a myosin-specific monoclonal antibody, or its Fab fragment, to produce bifunctional polychelants. . .

.

chelant moieties in the polychelants of the invention may be residues of any of the conventional macrocyclic chelants such as for example DOTA, TETA, D03A. etc, The macrocyclic skeleton, as mentioned above, preferably has 9 to 25 ring members and conveniently is an optionally oxygen or. . . pendent groups which participate in metal chelation, for example C1-6alkyl groups carrying hydroxyl, amino, phosphonate, or phosphinate or more preferably carboxyl groups. D03A and DOTA derived macrocycles are especially preferred, i,e. groups of formula
HOOC--\F-] X]--COOH HOOC--\F7 /-COOH
N N-] and [-N
EN N N N
\-COOH HOOC--/. . .

Exemplary polyazacycloalkanepolycarboxylates include 1 7,10-tetraazacyclododecanetetraacetic acid (DOTA), 1,4,7,10-tetraazacyclododecane 4,7-triacetic acid (DO3A), 1-oxa-4,7,10-triazacyclododecanetriacetic acid (DOXA), 1,4,7-triazacyclononanetriacetic acid (NOTA) and 1 8,11-tetraazacyclotetradecanetetraacetic acid (TETA), Additionally, the novel tetraazacycloalkanepolycarboxylates, DOTA-N(2-aminoethyl)amide and DOTA-N(4-aminophenethyl)amide are also contemplated,
The preparation of the tetraazacycloalkanepoly-carboxylate ligands is well known. Synthesis of DOTA is described in U.S. Patent No. 4,647,447 (Gries et al,), U.S. Patent No, 4,639,365 (Sherry) and by Desreux et al.

in Inorg. Chem. 19:1319 (1980). Additionally, DOTA is available commercially from Parish Chemical Co,, Orem, UT, USA. Preparation of D03A is described in EP-A-292689 (Squibb). Desreux, Inorg. Chem., 19:1319. . . al, Inorg. Chem, 26:3458 (1987)
and Meares et al, Acc. Chem. Res., 17:202 (1984) describe the properties and chemistry of tne macrocyclic ligands DOTA, NOTA, TETA and their backbone-derivatized analogues, including the preparation of NOTA and TETA.

U.S. Patent No, 4,678,667 (Meares et al.) teaches the preparation of a number of macrocyclic, side chain-derivatized ligands including DOTA and TETA.

Derivatization of DOTA to form DOTA
-N(2-aminoethyl)amide
and DOTA-N(4-aminophenethyl)amide is described in detail hereinafter in Examples 2 and 3, respectively, The above cited references and all other references mentioned herein are hereby. . .

.

be taken with the lanthanide ions to maintain the pH below 8 to avoid precipitation of the metal hydroxide. Metal incorporation into DOTA derived and related macrocylic chelant moieties will normally be a slow process, as described in the references cited below. Specific examples of the. . .

Med., 3:808 (1986) and WO-A-87/06229 describe

incorporation of Gd(III) into DOTA. A method of preparing Bi and Pb complexes of DOTA is described by Kumar et al, J. Chem. Soc. Chem. Commun., 3:145 (1989).

. . .

reduction of 99Tc with Sn in the presence of a weakly coordinating ligand such as glucoheptonate prior to complexation with chelants such as DOTA. These methods are well known in the radiopharmaceutical art 67CU utilizes tetraamine chelates such as tet A or tet B (see Bhardaredj. . .

CCK and hexapeptides), proteins (such as lectins, asialofetuin, polyclonal IgG, blood clotting proteins (e.g. hirudin), lipoproteins and glycoproteins), hormones, growth factors, and clotting factors. . .

. . .

In general, known methods can be used to join the macrocyclic chelants to backbone molecules. While for preferred macrocyclic chelants, such as DOTA, the conventional mixed anhydride and cyclic anhydride conjugation techniques are ineffective, it has been found that.modifying the mixed anhydride procedure by reacting a polycarboxylic. . .

For macrocycles with a pendant carboxylate, including but not limited to DOTA, TETA, TRITA (1,4,7,10-tetraazacyclotridecanetetraacetic acid) and NOTA, one of the carboxylates can form an entity which can react with a primary amine group. . .

. . .

linked to a backbone molecule through a non-coordinating primary amine group. Macrocyclic chelants having a non-coordinating primary amine group include primary amine side-chain-derivatized DOTA macrocycles, primary amine-derivatized D03A, and primary amine-derivatized hexaaza and octaaza macrocycles and macrobicycles (the HAMs.

. . .

for example, physiologically biocompatible buffers (as for example, tromethamine hydrochloride), additions (e,g,, 0.01 to 10 mole percent) of chelants (such as, for example, DTPA, DTPA-bisamide or non-complexed magnifier polychelant) or calcium chelate complexes (as for example calcium DTPA, CaNaDTPA-bisamide, calcium-magnifier polychelant or CaNa salts of magnifier polychelants), or, optionally, additions (e.g., 1 to 50 mole percent) of calcium or sodium salts (for. . .

L38 ANSWER 4 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1995005842 PCTFULL ED 20020514
TITLE (ENGLISH): METHOD AND DEVICE FOR TREATING GASTROINTESTINAL MUSCLE DISORDERS AND OTHER SMOOTH MUSCLE DYSFUNCTION
TITLE (FRENCH): PROCEDE ET DISPOSITIF POUR TRAITER LES TROUBLES MUSCULAIRES GASTRO-INTESTINAUX ET AUTRES DYSFONCTIONNEMENTS DES MUSCLES LISSES
INVENTOR(S): PASRICHA, Pankaj, J.;
KALLOO, Anthony, N.
PATENT ASSIGNEE(S): THE JOHNS HOPKINS UNIVERSITY
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9505842	A1	19950302

DESIGNATED STATES
W: CA JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
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DETD Figs. 3A and B show the effect of intrasphincteric injection of BoTx on LES response to cholecystokinin octapeptide (CCK)

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response of the LES to the IV administration of edrophonium (Tensilon; ICN Pharmaceuticals Inc., Costa Mesa, CA) and cholecystokinin octapeptide (CCK-8) (Kinevac; ER Squibb amp;Sons, Princeton, NJ) in three
additional piglets was also measured. LES pressures, measured by a DENTSLEEVE, were recorded in response to IV edrophonium (5 mg). After a SUBSTITUTE SHEET (RULE 26)
washout period of 10 minutes, CCK (5 µg IV) was then administered.
Subsequently, BoTx was injected into the LES, as described above, and the
experiment was. . .

Intrasphincteric BoTx also altered the response of the LES to CCK
(Figure 3). In untreated piglets, CCK did not cause any significant change in
LES pressure. However, after intrasphincteric BoTx injection, a significant
increase in LES pressure was seen in response to CCK. It should be noted that
despite what was felt to be an adequate washout period (10 minutes) in between
injections, basal. . .

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retention studies
After an overnight fast, patients were asked to ingest a corn-flake meal with milk containing 0.531 mci 99 aiTc DTPA. Subsequently, serial dynamic
images were obtained with the subject sitting erect in front of a gamma camera.
Retention was expressed. . .

L38 ANSWER 5 OF 5 PCTFULL COPYRIGHT 2006 Univentio on STN
ACCESSION NUMBER: 1993006868 PCTFULL ED 20020513
TITLE (ENGLISH): DENDRIMERIC POLYCHELANTS
TITLE (FRENCH): POLYCHELATEURS DENDRIMERES
INVENTOR(S): WATSON, Alan, D.
PATENT ASSIGNEE(S): COCKBAIN, Jilian, Roderick, Michaelson;
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WATSON, Alan, D.
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W: AU BB BG BR CA CS FI HU JP KP KR LK MG MN MW NO PL RO RU SD US AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE BF BJ CF CG CI CM GA GN ML MR SN TD TG
APPLICATION INFO.: WO 1992-EP2308 A 19921006
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ABEN . . . chelates which are useful in diagnostic imaging and in radiotherapy and which comprise a plurality of macrocyclic chelant moieties, e.g. DOTA
residues, conjugated to an up to fifth generation dendrimer backbone

molecule, e.g. a starburst
dendrimer. To produce a site-specific polychelate,. . .

ABFR . . . utilises dans l'imagerie diagnostique et en radiotherapie. Ils comportent une pluralite de fractions de chelateurs macrocycliques, par exemple
des restes DOTA, conjugues a une molecule de squelette dendrimere dont la generation va jusqu'a la cinquieme, par exemple un dendrimere en etoile.. . .

DETD . . . paramagnetic metal ion
chelates of bifunctional chelants for use as MRI contrast agents,
Thus, Krejcarek et al (supra) disclosed how polyaminopolycarboxylic acid (PAPCA) chelants, specifically DTPA (diethylepetriaminepentaacetic acid) could be conjugated to a protein, such as human serum albumin (HSA), by reaction of the triethylamine salt of the PAPCA. . .

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152:571 (1988))e
Unger et al, in Investigative Radiology 20:693 (1985) analyzed tumor enhancement for magnetic resonance imaging using an anti-CEA monoclonal antibody conjugated with Gd-DTPA* They found no tumor enhancement when 4 Gd atoms were bound per antibody molecule, and predicted that a far greater ratio of. . .

Thus Hnatowich et al, (supra) used the cyclic anhydride of the chelant DTPA to attach it to a protein, This, is a relatively simple one-step synthesis procedure which as a result has been used by. . .

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has
thus been used to produce bifunctional polychelants in which the chelant moieties are residues of open chain PAPCAs,, such as EDTA and DTPA,, and in which the backbone molecule is a polyamine such as polylysine or polyethyleneimine. Thus for example Manabe et al, in Biochemica. et Biophysica Acta 883: 460-467 (1986) reported attaching up to 105 DTPA residues onto a poly-L-lysine backbone using the cyclic anhydride method and also attaching polylysine-polyDTPA polychelants onto monoclonal antibody (anti-HLA IgGj) using a 2-pyridyl disulphide linker achieving a substitution of up to about 42,5 chelants (DTPA residues) per site-specific macromolecule. Torchlin et al. in Hybridoma 6:229-240 (1987) also reported attaching DTPA and EDTA to polyethyleneimine and polylysine backbones which were then attached to a myosin-specific monoclonal antibody, or its Fab fragment, to produce bifunctional polychelants. . .

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diagnosis and therapy, due in part
to their unique localization in the body, The monomeric chelates presently used for MRI contrast enhancement (e.g,, Gd(DTPA)2-,, Gd(DOTA)'-) have in vivo applications
related to their specific, rapid biodistribution, localizing these chelates in the extravasculari extracellular spaces of the body. The size. . .

Exemplary polyazacycloalkanepolycarboxylates include 1,4,7,10-tetraazacyclododecanetetraacetic acid (DOTA), 1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid (DO3A), I-oxa-4,7,10-triazacyclododecanetriacetic

acid (DOXA), 1.4,7-triazacyclononanetriacetic acid (NOTA) and 1.4,8,11-tetraazacyclotetradecanetetraacetic acid (TETA), Additionally, the novel - tetraazacycloalkanepolycarboxylates, DOTA-N(2-aminoethyl)amide and DOTA-N(4-aminophenethyl)amide are also contemplated.

The preparation of,the tetraazacycloalkanepoly-carboxylate ligands is well known. Synthesis of DOTA is described in U,S. Patent No, 4,647,447 (Gries et al,), U.S, Patent No, 4,639,365 (Sherry) and by Desreux et al, in Inorg. Chem, .19:1319 (1980). Additionally, DOTA is available commercially from Parrish Chemical Co,, Orem, UT, USA. Preparation of D03A is described in EP-A-292689 (Squibb). Desreux, Inorg. Chem,, 19:1319. . . et al, Inorg, Chem, 26:3458 (1987)
and Meares et al, Acc, Chem, Res,, 17:202 (1984) describe theproperties and chemistry of the macrocyclic ligands DOTA, NOTA, TETA and their backbone-derivatized analogues, including the preparation of NOTA and TETA, U.S. Patent No. 4,678,667 (Meares et al,) teaches the preparation of a number of macrocyclic, side chain-derivatized ligands including DOTA and TETA, Derivatization of DOTA to form DOTA -N(2-aminoethyl)amide
and DOTA-N(4-aminophenethyl)amide is described in detail hereinafter in Examples 2 and 3, respectively. The above cited references and all other references mentioned herein are hereby. . .

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acids, oligopeptides (e.g. hexapeptides), molecular recognition units (MRU's), single chain antibodies (SCA's), proteins, Fab fragments, and antibodies. Examples of site-directed molecules include polysaccharides (e,g, CCK and hexapeptides), proteins (such as lectins, asialofetuin, polyclonal IgG, blood clotting proteins (e.g. hirudin), lipoproteins and glycoproteins), hormones, growth factors, and clotting factors (such. . .

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molecule
in general, known methods can be used to join the macrocyclic chelants to backbone molecules. While for preferred macrocyclic chelants, such as DOTA, the conventional mixed anhydride and cyclic anhydride conjugation techniques are ineffective, it has been found that modifying the mixed anhydride procedure by reacting a. . .

For macrocycles with a pendant carboxylate, including but not limited to DOTA, TETA, TRITA (1.4,7,10-tetraazacyclotridecanetetraacetic acid) and NOTA, one of the carboxylates can form an entity which can react with a primary amine group of. . .

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linked to the
backbone polymer through a non-coordinating primary amine group. Macrocyclic chelants having a non-coordinating primary amine group include primary amine side-chain-derivatized DOTA macrocycles, primary amine-derivatized D03A. and primary amine-derivatized hexaaza and octaaza. macrocycles and macrobicycles (the HAMsr sepulchrates and sarcophagines) as well as the. . .

Metal incorporation into DOTA derived and related

macrocylic chelant moieties will normally be a slow process, as described in the references cited below, Specific examples of the. . .

Ned,, 3:808 (1986) and WO-A-87/06229 describe incorporation of Gd(III) into DOTA, A method of preparing Bi and Pb complexes of DOTA is described by Kumar et alf J. Chem, Soc, Chem, Commun., 3:145 (1989)o The above references are incorporated herein by reference in their. . .

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reduction of 99mTc
with Sn in the presence of a weakly coordinating ligand such as glucoheptonate prior to complexation with chelants such as DOTA, These methods are well known in the radiopharmaceutical art. OCu utilizes tetraamine chela]tes such as tet A or tet B (see Bhardaredj. . .

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for example, physiologically biocompatible buffers (as for example, tromethamine hydrochloride), additions (e.g., 0,01 to 10 mole percent) of chelants (such as, for example, DTPA, DTPA
-
bisamide or non-complexed magnifier polychelant) or calcium chelate complexes (as for example calcium DTPA, CaNaDTPA-bisamide, calcium-magn-ifier polychelant or CaNa salts of magnifier polychelants),, or, optionally, additions (e.g., I to 50 mole percent) of calcium or sodium salts (for. . .

EXAMPLE I
Preparation of DOTA Carboxycarbonic Anhydride
DOTA(0*808 g-I 2,0 mmol) was suspended in 5.0 ml of anhydrous acetonitrile, Tetramethylguanidine (1eOO mli, 8.0 mmol) was added and the mixture stirred under an atmosphere of nitrogen for about 5 minutes at ambient temperature until the DOTA was dissolved, The resulting solution was cooled to -250C under an atmosphere of nitrogen and stirred while adding 0,260 ml (2,0 mmol). . .

The resulting slurry was stirred for I hour at -25 C4
EXAMPLE 2
Preparation of DOTA-N(2-aminoethV1)amide
To the cold slurry from Example 1 was added a solution of mono-BOC-ethylenediamine (0,320g, 2mmol) in 2 ml acetonitrile and the mixture stirred. . . afforded 0.35g of a semi-
crystalline glass. IH NMR demonstrated the expected product, as well as some residual acetate (from chromatography),
EXAMPLE 3
Preparation of DOTA-N(4-aminoDhenethvl)amide
To the cold slurry from Example 1 is added a solution of 4-nitrophenethylamine (0,332g, 2mmol) in 4.0 ml acetonitrile, The mixture is stirred. . . and pH adjusted to 1015 with NaOH to form a mixture which is extracted with ethyl acetate to remove unreacted amine, The product,
DOTA-N-(41-nitrophenethyl)amide, is isolated by ion exchange chromatography on DOWEX AGI-XS resin.

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ceases to drop, The product is isolated by filtering off catalyst and evaporating the filtrate to dryness,
EXAMPLE 4
Activation of Amino Group of DOTA-N(2-aminoethyl)amide